A GENE AND USES THEREFOR

BACKGROUND OF THE INVENTION

FIELD OF THE INVENTION

The present invention relates generally to nucleic acid molecules identified by a pattern of their expression in at least the hypothalamus or skeletal muscle. Conveniently, the nucleic acid molecules are identified using differential display techniques under differing physiological conditions. The nucleic acid molecules are associated with or act as markers for conditions of *inter alia* a healthy or unhealthy state, including the presence or absence of a disorder associated with mitochondrial dysfunction, a myopathy, a genetic disorder and/or a cancer. More particularly, the present invention is directed to a nucleic acid molecule and/or its expression product for use in therapeutic and diagnostic protocols for conditions such as *inter alia* a disorder associated with mitochondrial dysfunction, a myopathy, a genetic disorder and/or a cancer. The subject nucleic acid molecule and expression product and their derivatives, homologs, analogs and mimetics are proposed to be useful, therefore, as therapeutic and diagnostic agents for *inter alia*, a disorder associated with mitochondrial dysfunction, a myopathy, a genetic disorder and/or a cancer or as targets for the design and/or identification of modulators of their activity and/or function. The subject nucleic acid molecule, therefore, are useful drug targets or targets for drug design or development.

DESCRIPTION OF THE PRIOR ART

Reference to any prior art in this specification is not, and should not be taken as, an acknowledgment or any form of suggestion that this prior art forms part of the common general knowledge in any country.

The increasing sophistication of recombinant DNA technology is greatly facilitating research and development in the veterinary and allied human and animal health fields. This

is particularly the case in the investigation of the genetic bases involved in the etiology of certain disease conditions. Diseases of particular concern include disorders associated with mitochondrial dysfunction as well as myopathies, genetic disorders and cancers.

Mitochondrial dysfunction refers to any illness resulting from a deficiency of any mitochondrial-located protein which is involved in energy metabolism. Therefore, deficiencies of the respiratory (electron transport) chain, either resulting from a deficiency in one or more of the mitochondrial or nuclear-encoded proteins, are mitochondrial disorders. Also, by definition, disorders of the fatty acid (beta) oxidation, Krebs cycle and pyruvate dehydrogenase complex deficiency are mitochondrial disorders. Although these disorders may be genetically dissimilar, mitochondrial dysfunction results in an energy deficient state.

There is no one identifying feature of mitochondrial disease. Subjects can have combinations of problems whose onset may occur from before birth to late adult life. Mitochondrial diseases should be considered in the differential diagnosis when there are unexplained features, especially when these occur in combination. Mitochondrial disease and disorders can affect multiple organs, resulting in a vast array of symptoms. Symptoms which may affect the brain include, developmental delays, mental retardation, dementia, seizures, neuro-psychiatric disturbances, atypical cerebral palsy, migraines, strokes.

Cancer is also one of the most debilitating disease conditions affecting predominantly humans but also a range of animals. The health cost to the world-wide community runs into the billions of dollars, let alone the personal cost to families.

Mitochondrial disease and cancer, therefore, are significant conditions requiring expenditure of time and financial resources to develop new methods of treatment, prevention and diagnosis.

In International Patent Application No. PCT/AU02/00109 [WO 02/062994], techniques including differential display analysis and macroarray (i.e. membrane-based microarray)

analysis of genetic material from hypothalamus tissue or muscle tissue were used to identify candidate genetic sequences associated with a healthy state or with physiological conditions such as obesity, anorexia, weight maintenance, diabetes, muscle development and/or metabolic energy levels. An animal model was employed comprising the Israeli Sand Rat (*Psammomys obesus*). Three groups of animals are used designated Groups A, B and C based on metabolic phenotype as follows:-

Group A: lean animals;
Group B: obese, non-diabetic animals; and
Group C: obese, diabetic animals.

Animals were maintained under two study conditions: (1) they were either fed *ad libitum* ("fed") or fasted for 24 hours ("fasted") prior to analysis; or (2) maintained by being fed *ad libitum* ("control") or placed on an energy restricted diet ("restricted"), and genetic sequences analyzed by differential display analysis. Using these techniques, differentially expressed sequences were identified from hypothalamus cells designated in AGT-106, AGT-113, AGT-201 and AGT-202. Another sequence, designated AGT-203, was differentially expressed in skeletal muscle.

In accordance with the present invention it is determined that the differentially expressed genetic sequences AGT-106, AGT-113, AGT-201, AGT202 and AGT-203 [as disclosed in International Publication No. WO 02/062994 and incorporated herein by reference] are useful markers and/or drug targets for mitochondrial dysfunction and other conditions such as myopathies, genetic disorders and cancers.

SUMMARY OF THE INVENTION

Throughout this specification, unless the context requires otherwise, the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated element or integer or group of elements or integers but not the exclusion of any other element or integer or group of elements or integers.

Nucleotide and amino acid sequences are referred to by a sequence identifier number (SEQ ID NO:). The SEQ ID NOs: correspond numerically to the sequence identifiers <400>1, <400>2, etc. A sequence listing is provided after the claims.

Differentially expressed nucleotide sequences are identified as being useful markers associated with mitochondrial dysfunction, myopathies, genetic disorders and/or cancers.

Differential expression means an elevation in levels of expression of a genetic sequence under one set of conditions compared to another. The differentially expressed nucleotide sequences are identified by "AGT" numbers. A summary of the AGT sequences disclosed in WO 02/062994 is provided in Table 1.

The identification of these variably expressed sequences permits the rationale design and/or selection of molecules capable of antagonizing or agonizing the expression products and/or permits the development of screening assays. The screening assays, for example, include assessing the physiological status of a particular subject. Furthermore, the screening assays are useful in drug target as well as drug evaluation.

Accordingly, one aspect of the present invention provides a nucleic acid molecule comprising a sequence of nucleotides encoding or complementary to a sequence encoding a protein or a derivative, homolog, analog or mimetic thereof wherein the nucleic acid molecule or its expression product is associated with one or more of mitochondrial dysfunction, myopathies, genetic disorders or cancers.

More particularly, the present invention contemplates a method for assessing the presence or absence of a mitochondrial dysfunction, myopathy, genetic disorder or cancer by determining the level of expression of a nucleic acid molecule which comprises a nucleotide sequence substantially as set forth in SEQ ID NO:1 or SEQ ID NO:2 or SEQ ID NO:3 or SEQ ID NO:4 or SEQ ID NO:5 or a nucleotide sequence having at least about 30% similarity to all or part of SEQ ID NO:1 or SEQ ID NO:2 or SEQ ID NO:3 or SEQ ID NO:4 or SEQ ID NO:5 and/or is capable of hybridizing to one or more of SEQ ID NO:1 or SEQ ID NO:2 or SEQ ID NO:3 or SEQ ID NO:4 or SEQ ID NO:5 or their complementary forms under low stringency conditions at 42°C.

The expression product molecule is generally a protein but may also be *inter alia* an mRNA, intron or exon.

The preferred genetic sequences of the present invention are referred to herein as *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203 (see Table 1)*. The expression products encoded by *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203* are referred to herein as AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203, respectively. As indicated above, the expression products may be an RNA (e.g. mRNA) or a protein. Where the expression produce is an RNA, the present invention extends to RNA-related molecules associated thereto such as RNAi.

A further aspect of the present invention relates to a composition comprising AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 or its derivatives, homologs, analogs or mimetics or agonists or antagonists of AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 together with one or more pharmaceutically acceptable carriers and/or diluents for use in treating conditions associated with mitochondrial dysfunction, myopathies, genetic disorders or cancer.

Furthermore, the present invention contemplates a method for treating a subject having mitochondrial dysfunction, myopathies, genetic disorders or cancer comprising administering to the subject, a treatment effective amount of AGT-106, AGT-113, AGT-

201, AGT-202 and AGT-203 or a derivative, homolog, analog or mimetic thereof or a genetic sequence encoding same or an agonist or antagonist of AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 or *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203* gene expression for a time and under conditions sufficient to effect treatment.

Treatment may be by the administration of a pharmaceutical composition or genetic sequences *via* gene therapy. Treatment is contemplated for human subjects as well as animals such as animals important to livestock industry.

Still another aspect of the present invention is directed to a diagnostic agent for use in monitoring or diagnosing conditions such as but not limited to a mitochondrial dysfunction, myopathies, genetic disorders or cancer, said diagnostic agent selected from an antibody or other ligand to AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 or its derivatives, homologs, analogs or mimetics and a genetic sequence useful in PCR, hybridization, RFLP, amongst other techniques. A particularly useful diagnostic agent is an antibody or genetic molecule which detects a level of expression of rhomboid-like protein (PSARL) the levels of PSARL is a useful indicator in kidney, breast, pancreas and cervical cancer.

A summary of sequence identifiers used throughout the subject specification is provided in Table 2. This Table is from WO 02/062994.

TABLE 1

Summary of Differentially Expressed Genes

GENE	SEQ ID NO:	TISSUE	PHENOTYPE	METHOD OF DETECTION
AGT-106	1	Hypothalamus	Higher expression in fed compared to fasted Sand rats (Group A [lean, healthy rats])	Differential display
AGT-113	2	Hypothalamus	Higher expression in Group C (obese, diabetic) compared to Group A	Differential display
AGT-201	3	Hypothalamus	Lower expression in fasted A and B (obese, normoglycemic and hyer-insulinemic) animals	Macroarray
AGT-202	4	Hypothalamus	Higher expression in fed compared to fasted animals in Group A and B compared to Group C animals	Differential display
AGT-203	5	Skeletal muscle	Higher expression in lean, non-diabetic (Group A) animals compared to (obese, diabetic) Group C	Macroarray

TABLE 2

Summary of Sequence Identifiers

SEQUENCE ID NO.	DESCRIPTION
1	Nucleotide sequence of *AGT-106*
2	Nucleotide sequence of *AGT-113*
3	Nucleotide sequence of *AGT-201*
4	Nucleotide sequence of AGT-202
5	Nucleotide sequence of Presenilins interacting rhomboid-like protein (AGT-203) (PSARL)
6	AGT-203 forward primer
7	AGT-203 reverse primer
8	AGT-203 probe
9	AGT-201 forward primer
10	AGT-201 reverse primer
11	AGT-201 probe
12	AGT-106 forward primer
13	AGT-106 reverse primer
14	AGT-202 forward primer
15	AGT-202 reverse primer
16	AGT-113 forward primer
17	AGT-113 reverse primer
18	Cyclophilin forward primer
19	Cyclophilin reverse primer
20	Cyclophilin probe

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention is predicated in part on the identification of genes associated *inter alia* with a mitochondrial dysfunction, a myopathy, a genetic disorder or a cancer. The genes were identified by a number of procedures including differential screening or macroarray analysis of hypothalamus or skeletal muscle mRNA between lean and obese animals normoglycemic (Shafrir and Gutman, *J Basic Clin Physiol Pharm 4:* 83-99, 1993) and/or between fed animals and fasted animals as disclosed in WO 02/062994.

Accordingly, one aspect of the present invention provides a nucleic acid molecule comprising a sequence of nucleotides encoding or complementary to a sequence encoding an expression product or a derivative, homolog, analog or mimetic thereof wherein said nucleic acid molecule is associated with one or more of mitochondrial dysfunction, myopathey, genetic disorder or cancer.

The term "differential" array is used in its broadest sense to include the expression of nucleic acid sequences in one type of tissue relative to another type of tissue in the same or different animals. Reference to "different" animals include the same animals but in different gastronomical states such as in a fed or non-fed state. Macroarray (i.e. membrane-based microarray) analysis preferably includes sets of arrays of nucleic and expression products (e.g. mRNA or PCR products) which display differential hybridization characteristics. An "animal" in this context includes a human or non-human animal.

It must be noted that, as used in the subject specification, the singular forms "a", "an" and "the" include plural aspects unless the context clearly dictates otherwise. Thus, for example, reference to a "gene" includes a single gene, as well as two or more genes; reference to "condition" includes a single condition, as well as two or more conditions and so forth.

The expression product may be a protein or mRNA or may be an exon or intron spliced, for example, from an RNA construct. The expression product may also be a hairpin

structure which induces or is associated with RNAi.

The altered expression levels may be in healthy animals or in lean, obese, diabetic or non-diabetic animals as disclosed in WO 02/062994.

The terms "lean" and "obese" are used in their most general sense but should be considered relative to the standard criteria for determining obesity. Generally, for human subjects, the definition of obesity is BMI>30 (Risk Factor Prevalence Study Management Committee. Risk Factor Prevalence Study: Survey No. 3 1989. Canberra: National Heart Foundation of Australia and Australian Institute of Health, 1990; Waters and Bennett, Risk Factors for cardiovascular disease: A summary of Australian data. Canberra: Australian Institute of Health and Welfare, 1995).

Conveniently, an animal model was employed to study the effects of obese and lean animals. In particular, WO 02/062994 exemplified differentially expressed genes using the *Psammomys obesus* (the Israeli sand rat) animal model of dietary-induced obesity and NIDDM. In its natural desert habitat, an active lifestyle and saltbush diet ensure that they remain lean and normoglycemic (Shafrir and Gutman, *J Basic Clin Physiol Pharm 4:* 83-99, 1993). However, in a laboratory setting on a diet of *ad libitum* chow (on which many other animal species remain healthy), a range of pathophysiological responses are seen (Barnett *et a.l, Diabetologia 37:* 671-676, 1994a; Barnett *et al., Int. J. Obesity 18:* 789-794, 1994b, Barnett *et al., Diabete Nutr Metab 8:* 42-47, 1995). By the age of 16 weeks, more than half of the animals become obese and approximately one third develop NIDDM. Only hyperphagic animals go on to develop hyperglycemia, highlighting the importance of excessive energy intake in the pathophysiology of obesity and NIDDM in *Psammomys obesus* (Collier *et al., Ann New York Acad Sci 827:* 50-63, 1997a; Walder *et al., Obesity Res 5:* 193-200, 1997a). Other phenotypes found include hyperinsulinemia, dyslipidemia and impaired glucose tolerance (Collier *et al.,* [1997a; *supra*]; Collier *et al., Exp Clin Endocrinol Diabetes 105:* 36-37, 1997b). *Psammomys obesus* exhibit a range of bodyweight and blood glucose and insulin levels which forms a continuous curve that closely resembles the patterns found in human populations, including the inverted U-

shaped relationship between blood glucose and insulin levels known as "Starling's curve of the pancreas" (Barnett *et al.*, [1994a; *supra*]). It is the heterogeneity of the phenotypic response of *Psammomys obesus* which make it an ideal model to study the etiology and pathophysiology of obesity and NIDDM.

Psammomys obesus animals are conveniently divided into three groups *viz* Group A animals which are lean, normoglycemic and normoinsulinemic, Group B animals which are obese, normoglycemic and hyperinuslinemic and Group C animals which are obese, hyperglycemic and hyperinsulinemic.

Another aspect of the present invention provides a method for assessing the presence or absence of a mitochondrial dysfunction, myopathy, genetic disorder or cancer by determining the level of expression of a nucleic acid molecule comprising a nucleotide sequence encoding or complementary to a sequence encoding an expression product or a derivative, homolog or mimetic thereof wherein said nucleotide sequence is as substantially set forth in SEQ ID NO:1 or SEQ ID NO:2 or SEQ ID NO:3 or SEQ ID NO:4 or SEQ ID NO:5 or a nucleotide sequence having at least about 30% similarity to all or part of SEQ ID NO:1 or SEQ ID NO:2 or SEQ ID NO:3 or SEQ ID NO:4 or SEQ ID NO:5 and/or is capable of hybridizing to one or more of SEQ ID NO:1 or SEQ ID NO:2 or SEQ ID NO:3 or SEQ ID NO:4 or SEQ ID NO:5 or their complementary forms under low stringency conditions at 42°C and wherein elevated or reduced levels of expression of one or more of these sequences is indicative of one or more of mitochondrial dysfunction, myopathy, genetic disorder or cancer.

Reference herein to similarity is generally at a level of comparison of at least 15 consecutive or substantially consecutive nucleotides or at least 5 consecutive or substantially consecutive amino acid residues. Preferred percentage similarities have at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 80% and at least about 90% or above. Examples include 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97,

98, 99 and 100%.

The term "similarity" as used herein includes exact identity between compared sequences at the nucleotide or amino acid level. Where there is non-identity at the nucleotide level, "similarity" includes differences between sequences which result in different amino acids that are nevertheless related to each other at the structural, functional, biochemical and/or conformational levels. Where there is non-identity at the amino acid level, "similarity" includes amino acids that are nevertheless related to each other at the structural, functional, biochemical and/or conformational levels. In a particularly preferred embodiment, nucleotide and sequence comparisons are made at the level of identity rather than similarity.

An expression product includes an RNA molecule such as a mRNA transcript as well as a protein. Some genes are non-protein encoding genes and produce mRNA or other RNA type molecules and are involved in regulation by RNA:DNA, RNA:RNA or RNA:protein interaction. The RNA (e.g. mRNA) may act directly or *via* the induction of other molecules such as RNAi or *via* products mediated from splicing events (e.g. exons or introns). Other genes encode mRNA transcripts which are then translated into proteins. A protein includes a polypeptide. The differentially expressed nucleic acid molecules, therefore, may encode mRNAs only or, in addition, proteins. Both mRNAs and proteins are forms of "expression products".

Terms used to describe sequence relationships between two or more polynucleotides or polypeptides include "reference sequence", "comparison window", "sequence similarity", "sequence identity", "percentage of sequence similarity", "percentage of sequence identity", "substantially similar" and "substantial identity". A "reference sequence" is at least 12 but frequently 15 to 18 and often at least 25 or above, such as 30 monomer units, inclusive of nucleotides and amino acid residues, in length, examples include 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24 and 25. Because two polynucleotides may each comprise (1) a sequence (i.e. only a portion of the complete polynucleotide sequence) that is similar between the two polynucleotides, and (2) a sequence that is divergent between

the two polynucleotides, sequence comparisons between two (or more) polynucleotides are typically performed by comparing sequences of the two polynucleotides over a "comparison window" to identify and compare local regions of sequence similarity. A "comparison window" refers to a conceptual segment of typically 12 contiguous residues that is compared to a reference sequence. The comparison window may comprise additions or deletions (i.e. gaps) of about 20% or less as compared to the reference sequence (which does not comprise additions or deletions) for optimal alignment of the two sequences. Optimal alignment of sequences for aligning a comparison window may be conducted by computerized implementations of algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package Release 7.0, Genetics Computer Group, 575 Science Drive Madison, WI, USA) or by inspection and the best alignment (i.e. resulting in the highest percentage homology over the comparison window) generated by any of the various methods selected. Reference also may be made to the BLAST family of programs as for example disclosed by Altschul *et al., Nucl. Acids Res. 25:* 3389, 1997. A detailed discussion of sequence analysis can be found in Unit 19.3 of Ausubel *et al.*, "Current Protocols in Molecular Biology" John Wiley & Sons Inc, 1994-1998, Chapter 15.

The terms "sequence similarity" and "sequence identity" as used herein refers to the extent that sequences are identical or functionally or structurally similar on a nucleotide-by-nucleotide basis or an amino acid-by-amino acid basis over a window of comparison. Thus, a "percentage of sequence identity", for example, is calculated by comparing two optimally aligned sequences over the window of comparison, determining the number of positions at which the identical nucleic acid base (e.g. A, T, C, G, I) or the identical amino acid residue (e.g. Ala, Pro, Ser, Thr, Gly, Val, Leu, Ilė, Phe, Tyr, Trp, Lys, Arg, His, Asp, Glu, Asn, Gln, Cys and Met) occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the window of comparison (i.e., the window size), and multiplying the result by 100 to yield the percentage of sequence identity. For the purposes of the present invention, "sequence identity" will be understood to mean the "match percentage" calculated by the DNASIS computer program (Version 2.5 for windows; available from Hitachi Software engineering Co., Ltd., South San Francisco, California, USA) using standard defaults as used in the

reference manual accompanying the software. Similar comments apply in relation to sequence similarity.

Reference herein to a low stringency includes and encompasses from at least about 0 to at least about 15% v/v formamide and from at least about 1 M to at least about 2 M salt for hybridization, and at least about 1 M to at least about 2 M salt for washing conditions. Generally, low stringency is at from about 25-30°C to about 42°C, such as 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41 and 42°C. The temperature may be altered and higher temperatures used to replace formamide and/or to give alternative stringency conditions. Alternative stringency conditions may be applied where necessary, such as medium stringency, which includes and encompasses from at least about 16% v/v to at least about 30% v/v formamide, such as 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 and 30% and from at least about 0.5 M to at least about 0.9 M salt, such as 0.5, 0.6, 0.7, 0.8 and 0.9 M for hybridization, and at least about 0.5 M to at least about 0.9 M salt, such as 0.5, 0.6, 0.7, 0.8 and 0.9 M for washing conditions, or high stringency, which includes and encompasses from at least about 31% v/v to at least about 50% v/v formamide, such as 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 and 50% v/v formamide and from at least about 0.01 M to at least about 0.15 M salt, such as 0.01, 0.02, 0.03, 0.04, 0.05, 0.06, 0.07, 0.08, 0.09, 0.10, 0.11, 0.12, 0.13, 0.14 and 0.15 M for hybridization, and at least about 0.01 M to at least about 0.15 M salt, such as 0.01, 0.02, 0.03, 0.04, 0.05, 0.06, 0.07, 0.08, 0.09, 0.10, 0.11, 0.12, 0.13, 0.14 and 0.15 M for washing conditions. In general, washing is carried out $T_m = 69.3 + 0.41$ (G+C)% (Marmur and Doty, *J. Mol. Biol. 5:* 109, 1962). However, the T_m of a duplex DNA decreases by 1°C with every increase of 1% in the number of mismatch base pairs (Bonner and Laskey, *Eur. J. Biochem. 46:*83, 1974). Formamide is optional in these hybridization conditions. Accordingly, particularly preferred levels of stringency are defined as follows: low stringency is 6 x SSC buffer, 0.1% w/v SDS at 25-42°C; a moderate stringency is 2 x SSC buffer, 0.1% w/v SDS at a temperature in the range 20°C to 65°C; high stringency is 0.1 x SSC buffer, 0.1% w/v SDS at a temperature of at least 65°C.

The nucleotide sequence or amino acid sequence of the present invention may correspond

to exactly the same sequence of the naturally occurring gene (or corresponding cDNA) or protein or may carry one or more nucleotide or amino acid substitutions, additions and/or deletions. The nucleotide sequences set forth in SEQ ID NO:1, SEQ ID NO:2 or SEQ ID NO:3 or SEQ ID NO:4 or SEQ ID NO:5 correspond to the genes referred to herein as *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203*, respectively. The corresponding expression products are AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203, respectively. Reference herein to *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203* includes, where appropriate, reference to the genomic gene or cDNA as well as any naturally occurring or induced derivatives. Apart from the substitutions, deletions and/or additions to the nucleotide sequence, the present invention further encompasses mutants, fragments, parts and portions of the nucleotide sequence corresponding to *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203*.

Another aspect of the present invention provides a nucleic acid molecule or derivative, homolog or analog thereof associated with one or more of mitochondrial dysfunction, myopathy, a genetic disorder or cancer said nucleic acid molecule comprising a nucleotide sequence encoding, or a nucleotide sequence complementary to a sequence encoding an expression product wherein said nucleotide sequence is substantially as set forth in SEQ ID NO:1 or a derivative, homolog or mimetic thereof or having at least about 40% identity to all or part of SEQ ID NO:1.

Yet another aspect of the present invention provides a nucleic acid molecule or derivative, homolog or analog thereof associated with one or more of mitochondrial dysfunction, myopathy, a genetic disorder or cancer said nucleic acid molecule comprising a nucleotide sequence encoding, or a nucleotide sequence complementary to a sequence encoding an expression product wherein said nucleotide sequence is substantially as set forth in SEQ ID NO:2 or a derivative, homolog or mimetic thereof or having at least about 40% identity to all or part of SEQ ID NO:2.

Still yet another aspect of the present invention provides a nucleic acid molecule or derivative, homolog or analog thereof associated with one or more of mitochondrial

dysfunction, myopathy, a genetic disorder or cancer said nucleic acid molecule comprising a nucleotide sequence encoding, or a nucleotide sequence complementary to a sequence encoding an expression product wherein said nucleotide sequence is substantially as set forth in SEQ ID NO:3 or a derivative, homolog or mimetic thereof or having at least about 40% identity to all or part of SEQ ID NO:3.

Another aspect of the present invention provides a nucleic acid molecule or derivative, homolog or analog thereof associated with one or more of mitochondrial dysfunction, myopathy, a genetic disorder or cancer said nucleic acid molecule comprising a nucleotide sequence encoding, or a nucleotide sequence complementary to a sequence encoding an expression product wherein said nucleotide sequence is substantially as set forth in SEQ ID NO:4 or a derivative, homolog or mimetic thereof or having at least about 40% identity to all or part of SEQ ID NO:4.

Another aspect of the present invention provides a nucleic acid molecule or derivative, homolog or analog thereof associated with one or more of mitochondrial dysfunction, myopathy, a genetic disorder or cancer said nucleic acid molecule comprising a nucleotide sequence encoding, or a nucleotide sequence complementary to a sequence encoding an expression product wherein said nucleotide sequence is substantially as set forth in SEQ ID NO:5 or a derivative, homolog or mimetic thereof or having at least about 40% identity to all or part of SEQ ID NO:5.

The expression pattern of *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203* has been determined, *inter alia*, to indicate an involvement in the regulation of one or more of a associated with one or more of mitochondrial dysfunction, myopathy, a genetic disorder or cancer said nucleic acid molecule. The subject nucleic acid molecules are preferably a sequence of deoxyribonucleic acids such as a cDNA sequence or a genomic sequence. A genomic sequence may also comprise exons and introns. A genomic sequence may also include a promoter region or other regulatory regions. The present invention extends, however, to expression products such as mRNA, introns and exons which may also be involved in genetic networking, whether or not they are translated into proteins.

Furthermore, the expression products may include complexes comprising RNA or may comprising RNAi or RNAi-type molecules.

A homolog is considered to be an *AGT-106, AGT-113, AGT-201, AGT-202* or *AGT-203* gene from another animal species. The *AGT-106, AGT-113, AGT-201, AGT-202* or *AGT-203* genes are exemplified in WO 02/062994 as being derived from *Psammomys obesus* hypothalamus. The present invention extends, however, to the homologous gene, as determined by nucleotide sequence and/or amino acid sequences and/or function, from primates, including humans, marmosets, orangutans and gorillas, livestock animals (e.g. cows, sheep, pigs, horses, donkeys, camels), laboratory test animals (e.g. mice, rats, guinea pigs, hamsters, rabbits), companion animals (e.g. cats, dogs) and captured wild animals (e.g. rodents, foxes, deer, kangaroos). The present invention also contemplates deimmunized forms of the expression products from one species relative to another species. In one preferred embodiment, the deimmunized form of the expression product is a mamalianized form relative to a particular target animal. In a most preferred embodiment where the target mammal is a human, the present invention contemplates use of a humanized form of a non-human expression product.

AGT-106, AGT-113, AGT-201, AGT-202 and *AGT-203* and its derivatives and homologs may be in isolated or purified form and/or may be ligated to a vector such as an expression vector. Expression may be in a eukaryotic cell line (e.g. mammalian, insect or yeast cells) or in microbial cells (e.g. *E. coli)* or both.

By "isolated" is meant a nucleic acid molecule having undergone at least one purification step and this is conveniently defined, for example, by a composition comprising at least about 10% subject nucleic acid molecule, preferably at least about 20%, more preferably at least about 30%, still more preferably at least about 40-50%, even still more preferably at least about 60-70%, yet even still more preferably 80-90% or greater of subject nucleic acid molecule relative to other components as determined by molecular weight, encoding activity, nucleotide sequence, base composition or other convenient means. The nucleic acid molecule of the present invention may also be considered, in a preferred embodiment,

to be biologically pure. The nucleic acid molecule may be ligated to an expression vector capable of expression in a prokaryotic cell (e.g. *E. coli*) or a eukaryotic cell (e.g. yeast cells, fungal cells, insect cells, mammalian cells or plant cells). The nucleic acid molecule may be ligated or fused or otherwise associated with a nucleic acid molecule encoding another entity such as, for example, a signal peptide. It may also comprise additional nucleotide sequence information fused, linked or otherwise associated with it either at the 3' or 5' terminal portions or at both the 3' and 5' terminal portions. The nucleic acid molecule may also be part of a vector, such as an expression vector.

The derivatives of the nucleic acid molecule of the present invention include oligonucleotides, PCR primers, antisense molecules, molecules suitable for use in co-suppression (e.g. RNAi) and fusion nucleic acid molecules. Ribozymes and DNA enzymes are also contemplated by the present invention directed to *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203* or its mRNA. Derivatives and homologs of *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203* are conveniently encompassed by those nucleotide sequences capable of hybridizing to SEQ ID NO:1, SEQ ID NO:2 or SEQ ID NO:3 or SEQ ID NO:4 or SEQ ID NO:5 or their complementary form under low stringency conditions.

The present invention extends to expression products of AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203. The preferred expression products are proteins or mutants, derivatives, homologs or analogs thereof as well as a range of RNA molecules.

Derivatives include fragments, parts, portions, mutants, variants and mimetics from natural, synthetic or recombinant sources including fusion proteins. Parts or fragments include, for example, active regions of AGT-106, AGT-113, AGT-202 or AGT-203. Derivatives may be derived from insertion, deletion or substitution of amino acids. Amino acid insertional derivatives include amino and/or carboxylic terminal fusions as well as intrasequence insertions of single or multiple amino acids. Insertional amino acid sequence variants are those in which one or more amino acid residues are introduced into a predetermined site in the protein although random insertion is also possible with suitable

screening of the resulting product. Deletional variants are characterized by the removal of one or more amino acids from the sequence. Substitutional amino acid variants are those in which at least one residue in the sequence has been removed and a different residue inserted in its place. An example of substitutional amino acid variants are conservative amino acid substitutions. Conservative amino acid substitutions typically include substitutions within the following groups: glycine and alanine; valine, isoleucine and leucine; aspartic acid and glutamic acid; asparagine and glutamine; serine and threonine; lysine and arginine; and phenylalanine and tyrosine. Additions to amino acid sequences include fusions with other peptides, polypeptides or proteins.

Chemical and functional equivalents of AGT-106, AGT-113, AGT-202 or AGT-203 should be understood as molecules exhibiting any one or more of the functional activities of these molecules and may be derived from any source such as being chemically synthesized or identified via screening processes such as natural product screening.

The derivatives include fragments having particular epitopes or parts of the entire protein fused to peptides, polypeptides or other proteinaceous or non-proteinaceous molecules.

Another aspect of the present invention provides an isolated protein or other expression product or a derivative, homolog, analog or mimetic thereof which is associated with one or more of mitochondrial disease, myopathy, a genetic disorder or cancer.

In a more preferred aspect of the present invention, there is provided an isolated protein or a derivative, homolog, analog or mimetic thereof or other expression product wherein said protein or expression product comprises an amino acid or nucleotide sequence substantially encoded by a nucleotide sequence as set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4 or SEQ ID NO:5 or an amino acid sequence having at least 30% similarity to all or part thereof and wherein said protein or expression product is associated with one or more of mitochondrial dysfunction, myopathy, a genetic disorder or cancer.

A further aspect of the present invention is directed to an isolated protein or a derivative, homolog, analog or mimetic thereof or other expression product wherein said protein or expression product is encoded by a nucleotide sequence substantially as set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4 or SEQ ID NO:5 or a nucleotide sequence having at least 30% similarity to all or part of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4 or SEQ ID NO:5 and/or is capable of hybridizing to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4 or SEQ ID NO:5 or their complementary forms under low stringency conditions at 42°C, wherein said protein or expression product is associated with a mitochondrial dysfunction, a myopathy, a genetic disorder or cancer.

Reference herein to AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 includes reference to isolated or purified naturally occurring AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 protein or expression product molecules as well as any derivatives, homologs, analogs and mimetics thereof. Derivatives include parts, fragments and portions of AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 as well as single and multiple amino acid substitutions, deletions and/or additions to AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203. A derivative of AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 is conveniently encompassed by molecules encoded by a nucleotide sequence capable of hybridizing to SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4 or SEQ ID NO:5 under low stringency conditions at 42°C.

Other derivatives of AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 include chemical analogs. Analogs of AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 contemplated herein include, but are not limited to, modifications to side chains, incorporation of unnatural amino acids and/or their derivatives during peptide, polypeptide or protein synthesis and the use of crosslinkers and other methods which impose confirmational constraints on the proteinaceous molecule or their analogs.

Examples of side chain modifications contemplated by the present invention include modifications of amino groups such as by reductive alkylation by reaction with an

aldehyde followed by reduction with $NaBH_4$; amidination with methylacetimidate; acylation with acetic anhydride; carbamoylation of amino groups with cyanate; trinitrobenzylation of amino groups with 2, 4, 6-trinitrobenzene sulphonic acid (TNBS); acylation of amino groups with succinic anhydride and tetrahydrophthalic anhydride; and pyridoxylation of lysine with pyridoxal-5-phosphate followed by reduction with $NaBH_4$.

The guanidine group of arginine residues may be modified by the formation of heterocyclic condensation products with reagents such as 2,3-butanedione, phenylglyoxal and glyoxal.

The carboxyl group may be modified by carbodiimide activation *via* O-acylisourea formation followed by subsequent derivitization, for example, to a corresponding amide.

Sulphydryl groups may be modified by methods such as carboxymethylation with iodoacetic acid or iodoacetamide; performic acid oxidation to cysteic acid; formation of a mixed disulphides with other thiol compounds; reaction with maleimide, maleic anhydride or other substituted maleimide; formation of mercurial derivatives using 4-chloromercuribenzoate, 4-chloromercuriphenylsulphonic acid, phenylmercury chloride, 2-chloromercuri-4-nitrophenol and other mercurials; carbamoylation with cyanate at alkaline pH.

Tryptophan residues may be modified by, for example, oxidation with N-bromosuccinimide or alkylation of the indole ring with 2-hydroxy-5-nitrobenzyl bromide or sulphenyl halides. Tyrosine residues on the other hand, may be altered by nitration with tetranitromethane to form a 3-nitrotyrosine derivative.

Modification of the imidazole ring of a histidine residue may be accomplished by alkylation with iodoacetic acid derivatives or N-carbethoxylation with diethylpyrocarbonate.

Examples of incorporating unnatural amino acids and derivatives during peptide synthesis include, but are not limited to, use of norleucine, 4-amino butyric acid, 4-amino-3-hydroxy-5-phenylpentanoic acid, 6-aminohexanoic acid, t-butylglycine, norvaline, phenylglycine, ornithine, sarcosine, 4-amino-3-hydroxy-6-methylheptanoic acid, 2-thienyl alanine and/or D-isomers of amino acids. A list of unnatural amino acid, contemplated herein is shown in Table 3.

TABLE 3

Non-conventional amino acid	Code	Non-conventional amino acid	Code
α-aminobutyric acid	Abu	L-N-methylalanine	Nmala
α-amino-α-methylbutyrate	Mgabu	L-N-methylarginine	Nmarg
aminocyclopropane-carboxylate	Cpro	L-N-methylasparagine	Nmasn
		L-N-methylaspartic acid	Nmasp
aminoisobutyric acid	Aib	L-N-methylcysteine	Nmcys
aminonorbornyl-carboxylate	Norb	L-N-methylglutamine	Nmgln
		L-N-methylglutamic acid	Nmglu
cyclohexylalanine	Chexa	L-Nmethylhistidine	Nmhis
cyclopentylalanine	Cpen	L-N-methylisolleucine	Nmile
D-alanine	Dal	L-N-methylleucine	Nmleu
D-arginine	Darg	L-N-methyllysine	Nmlys
D-aspartic acid	Dasp	L-N-methylmethionine	Nmmet
D-cysteine	Dcys	L-N-methylnorleucine	Nmnle
D-glutamine	Dgln	L-N-methylnorvaline	Nmnva
D-glutamic acid	Dglu	L-N-methylornithine	Nmorn
D-histidine	Dhis	L-N-methylphenylalanine	Nmphe
D-isoleucine	Dile	L-N-methylproline	Nmpro
D-leucine	Dleu	L-N-methylserine	Nmser
D-lysine	Dlys	L-N-methylthreonine	Nmthr
D-methionine	Dmet	L-N-methyltryptophan	Nmtrp
D-ornithine	Dorn	L-N-methyltyrosine	Nmtyr
D-phenylalanine	Dphe	L-N-methylvaline	Nmval
D-proline	Dpro	L-N-methylethylglycine	Nmetg
D-serine	Dser	L-N-methyl-t-butylglycine	Nmtbug
D-threonine	Dthr	L-norleucine	Nle
D-tryptophan	Dtrp	L-norvaline	Nva

D-tyrosine	Dtyr	α-methyl-aminoisobutyrate	Maib
D-valine	Dval	α-methyl-γ-aminobutyrate	Mgabu
D-α-methylalanine	Dmala	α-methylcyclohexylalanine	Mchexa
D-α-methylarginine	Dmarg	α-methylcylcopentylalanine	Mcpen
D-α-methylasparagine	Dmasn	α-methyl-α-napthylalanine	Manap
D-α-methylaspartate	Dmasp	α-methylpenicillamine	Mpen
D-α-methylcysteine	Dmcys	N-(4-aminobutyl)glycine	Nglu
D-α-methylglutamine	Dmgln	N-(2-aminoethyl)glycine	Naeg
D-α-methylhistidine	Dmhis	N-(3-aminopropyl)glycine	Norn
D-α-methylisoleucine	Dmile	N-amino-α-methylbutyrate	Nmaabu
D-α-methylleucine	Dmleu	α-napthylalanine	Anap
D-α-methyllysine	Dmlys	N-benzylglycine	Nphe
D-α-methylmethionine	Dmmet	N-(2-carbamylethyl)glycine	Ngln
D-α-methylornithine	Dmorn	N-(carbamylmethyl)glycine	Nasn
D-α-methylphenylalanine	Dmphe	N-(2-carboxyethyl)glycine	Nglu
D-α-methylproline	Dmpro	N-(carboxymethyl)glycine	Nasp
D-α-methylserine	Dmser	N-cyclobutylglycine	Ncbut
D-α-methylthreonine	Dmthr	N-cycloheptylglycine	Nchep
D-α-methyltryptophan	Dmtrp	N-cyclohexylglycine	Nchex
D-α-methyltyrosine	Dmty	N-cyclodecylglycine	Ncdec
D-α-methylvaline	Dmval	N-cylcododecylglycine	Ncdod
D-N-methylalanine	Dnmala	N-cyclooctylglycine	Ncoct
D-N-methylarginine	Dnmarg	N-cyclopropylglycine	Ncpro
D-N-methylasparagine	Dnmasn	N-cycloundecylglycine	Ncund
D-N-methylaspartate	Dnmasp	N-(2,2-diphenylethyl)glycine	Nbhm
D-N-methylcysteine	Dnmcys	N-(3,3-diphenylpropyl)glycine	Nbhe
D-N-methylglutamine	Dnmgln	N-(3-guanidinopropyl)glycine	Narg
D-N-methylglutamate	Dnmglu	N-(1-hydroxyethyl)glycine	Nthr
D-N-methylhistidine	Dnmhis	N-(hydroxyethyl))glycine	Nser
D-N-methylisoleucine	Dnmile	N-(imidazolylethyl))glycine	Nhis

D-N-methylleucine	Dnmleu	N-(3-indolylyethyl)glycine	Nhtrp
D-N-methyllysine	Dnmlys	N-methyl-γ-aminobutyrate	Nmgabu
N-methylcyclohexylalanine	Nmchexa	D-N-methylmethionine	Dnmmet
D-N-methylornithine	Dnmorn	N-methylcyclopentylalanine	Nmcpen
N-methylglycine	Nala	D-N-methylphenylalanine	Dnmphe
N-methylaminoisobutyrate	Nmaib	D-N-methylproline	Dnmpro
N-(1-methylpropyl)glycine	Nile	D-N-methylserine	Dnmser
N-(2-methylpropyl)glycine	Nleu	D-N-methylthreonine	Dnmthr
D-N-methyltryptophan	Dnmtrp	N-(1-methylethyl)glycine	Nval
D-N-methyltyrosine	Dnmtyr	N-methyla-napthylalanine	Nmanap
D-N-methylvaline	Dnmval	N-methylpenicillamine	Nmpen
γ-aminobutyric acid	Gabu	N-(*p*-hydroxyphenyl)glycine	Nhtyr
L-*t*-butylglycine	Tbug	N-(thiomethyl)glycine	Ncys
L-ethylglycine	Etg	penicillamine	Pen
L-homophenylalanine	Hphe	L-α-methylalanine	Mala
L-α-methylarginine	Marg	L-α-methylasparagine	Masn
L-α-methylaspartate	Masp	L-α-methyl-*t*-butylglycine	Mtbug
L-α-methylcysteine	Mcys	L-methylethylglycine	Metg
L-α-methylglutamine	Mgln	L-α-methylglutamate	Mglu
L-α-methylhistidine	Mhis	L-α-methylhomophenylalanine	Mhphe
L-α-methylisoleucine	Mile	N-(2-methylthioethyl)glycine	Nmet
L-α-methylleucine	Mleu	L-α-methyllysine	Mlys
L-α-methylmethionine	Mmet	L-α-methylnorleucine	Mnle
L-α-methylnorvaline	Mnva	L-α-methylornithine	Morn
L-α-methylphenylalanine	Mphe	L-α-methylproline	Mpro
L-α-methylserine	Mser	L-α-methylthreonine	Mthr
L-α-methyltryptophan	Mtrp	L-α-methyltyrosine	Mtyr
L-α-methylvaline	Mval	L-N-methylhomophenylalanine	Nmhphe
N-(N-(2,2-diphenylethyl) carbamylmethyl)glycine	Nnbhm	N-(N-(3,3-diphenylpropyl) carbamylmethyl)glycine	Nnbhe

1-carboxy-1-(2,2-diphenyl-ethylamino)cyclopropane	Nmbc

Crosslinkers can be used, for example, to stabilize 3D conformations, using homo-bifunctional crosslinkers such as the bifunctional imido esters having $(CH_2)_n$ spacer groups with n=1 to n=6, glutaraldehyde, N-hydroxysuccinimide esters and hetero-bifunctional reagents which usually contain an amino-reactive moiety such as N-hydroxysuccinimide and another group specific-reactive moiety such as maleimido or dithio moiety (SH) or carbodiimide (COOH). In addition, peptides can be conformationally constrained by, for example, incorporation of C_α and N $_\alpha$-methylamino acids, introduction of double bonds between C_α and C_β atoms of amino acids and the formation of cyclic peptides or analogs by introducing covalent bonds such as forming an amide bond between the N and C termini, between two side chains or between a side chain and the N or C terminus.

All such modifications may also be useful in stabilizing the AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 molecule for use in *in vivo* administration protocols or for diagnostic purposes.

As stated above, the expression product may be an RNA or protein.

The term "protein" should be understood to encompass peptides, polypeptides and proteins. The protein may be glycosylated or unglycosylated and/or may contain a range of other molecules fused, linked, bound or otherwise associated to the protein such as amino acids, lipids, carbohydrates or other peptides, polypeptides or proteins. Reference hereinafter to a "protein" includes a protein comprising a sequence of amino acids as well as a protein associated with other molecules such as amino acids, lipids, carbohydrates or other peptides, polypeptides or proteins.

In a particularly preferred embodiment, the expression product is encoded by a sequence of nucleotides as set forth in SEQ ID NO:1 or a derivative, homolog or analog thereof including a nucleotide sequence having at least about 40% identity to SEQ ID NO:1.

In another particularly preferred embodiment, the expression product is encoded by a sequence of nucleotides as set forth in SEQ ID NO:2 or a derivative, homolog or analog thereof including a nucleotide sequence having at least about 40% identity to SEQ ID NO:2.

In still another particularly preferred embodiment, the expression product is encoded by a sequence of nucleotides as set forth in SEQ ID NO:3 or a derivative homolog or analog thereof including a nucleotide sequence having at least about 40% identity to SEQ ID NO:3.

In still another particularly preferred embodiment, the expression product is encoded by a sequence of nucleotides as set forth in SEQ ID NO:4 or a derivative homolog or analog thereof including a nucleotide sequence having at least about 40% identity to SEQ ID NO:4.

In still another particularly preferred embodiment, the expression product is encoded by a sequence of nucleotides as set forth in SEQ ID NO:5 or a derivative homolog or analog thereof including a nucleotide sequence having at least about 40% identity to SEQ ID NO:5.

Higher similarities are also contemplated by the present invention such as greater than 40% or 50% or 60% or 70% or 80% or 90% or 95% or 96% or 97% or 98% or 99% or above. Further examples include 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 and 100%.

Another aspect of the present invention is directed to an isolated expression product associated with one or more of mitochondrial dysfunction, myopathy, a genetic disorder or cancer, said expression product selected from the list consisting of:-

(i) an mRNA or protein encoded by a novel nucleic acid molecule which molecule is differentially expressed in hypothalamus tissue of obese animals compared to lean *Psammomys obesus* animals or a derivative, homolog, analog, chemical equivalent or mimetic thereof;

(ii) an mRNA or protein encoded by a novel nucleic acid molecule which molecule is differentially expressed in hypothalamus tissue of fasted animals compared to fed *Psammomys obesus* animals or a derivative, homolog, analog, chemical equivalent or mimetic thereof;

(iii) *AGT-106 AGT-113, AGT-201, AGT-202* and *AGT-203* or a derivative, homolog, analog, chemical equivalent or mimetic thereof;

(iv) a protein encoded by a nucleotide sequence substantially as set forth in SEQ ID NO:1 or a derivative, homolog or analog thereof or a sequence encoding an amino acid sequence having at least about 40% similarity to this sequence or a derivative, homolog, analog, chemical equivalent or mimetic of said protein;

(v) a protein encoded by a nucleotide sequence substantially as set forth in SEQ ID NO:2 or a derivative, homolog or analog thereof or a sequence encoding an amino acid sequence having at least about 40% similarity to this sequence or a derivative, homolog, analog, chemical equivalent or mimetic of said protein;

(vi) a protein encoded by a nucleotide sequence substantially as set forth in SEQ ID NO:3 or a derivative, homolog or analog thereof or a sequence encoding an amino acid sequence having at least about 40% similarity to this sequence or a derivative, homolog, analog, chemical equivalent or mimetic of said protein;

(vii) a protein encoded by a nucleotide sequence substantially as set forth in SEQ ID NO:4 or a derivative, homolog or analog thereof or a sequence encoding an amino acid sequence having at least about 40% similarity to this sequence or a derivative, homolog, analog, chemical equivalent or mimetic of said protein; and

(viii) a protein encoded by a nucleotide sequence substantially as set forth in SEQ ID NO:5 or a derivative, homolog or analog thereof or a sequence encoding an amino acid sequence having at least about 40% similarity to this sequence or a derivative, homolog, analog, chemical equivalent or mimetic of said protein.

In a particularly preferred embodiment, the nucleotide sequence corresponding to *AGT-106* is a cDNA sequence comprising a sequence of nucleotides as set forth in SEQ ID NO:1 or a derivative, homolog or analog thereof including a nucleotide sequence having similarity to SEQ ID NO:1.

In another particularly preferred embodiment, the nucleotide sequence corresponding to *AGT-113* is a cDNA sequence comprising a sequence of nucleotides as set forth in SEQ ID NO:2 or a derivative, homolog or analog thereof including a nucleotide sequence having similarity to SEQ ID NO:2.

In still another particularly preferred embodiment, the nucleotide sequence corresponding to *AGT-201* is a cDNA sequence comprising a sequence of nucleotides as set forth in SEQ ID NO:3 or a derivative, homolog or analog thereof including a nucleotide sequence having similarity to SEQ ID NO:3.

In a further particularly preferred embodiment, the nucleotide sequence corresponding to *AGT-202* is a cDNA sequence comprising a sequence of nucleotides as set forth in SEQ ID NO:4 or a derivative, homolog or analog thereof including a nucleotide sequence having similarity to SEQ ID NO:4.

In still a further particularly preferred embodiment, the nucleotide sequence corresponding to *AGT-203* is a cDNA sequence comprising a sequence of nucleotides as set forth in SEQ ID NO:5 or a derivative, homolog or analog thereof including a nucleotide sequence having similarity to SEQ ID NO:5.

The nucleic acid molecule may be ligated to an expression vector capable of expression in a prokaryotic cell (e.g. *E.coli*) or a eukaryotic cell (e.g. yeast cells, fungal cells, insect cells, mammalian cells or plant cells). The nucleic acid molecule may be ligated or fused or otherwise associated with a nucleic acid molecule encoding another entity such as, for example, a signal peptide. It may also comprise additional nucleotide sequence information fused, linked or otherwise associated with it either at the 3' or 5' terminal portions or at both the 3' and 5' terminal portions. The nucleic acid molecule may also be part of a vector, such as an expression vector. The latter embodiment facilitates production of recombinant forms of sphingosine kinase which forms are encompassed by the present invention.

The present invention extends to the expression product of the nucleic acid molecules as hereinbefore defined. The expression product is preferably a protein but extends to mRNA, RNA, introns and exons.

Preferably, the expression products are AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 encoded by SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4 or SEQ ID NO:5, respectively or are derivatives, analogs, homologs, chemical equivalents or mimetics thereof.

Another aspect of the present invention is directed to an isolated protein associated with one or more of mitochondrial dysfunction, myopathy, a genetic disorder or cancer, said protein selected from the list consisting of:-

(i) an mRNA or a protein encoded by a nucleic acid molecule which molecule is differentially expressed in hypothalamus or muscle tissue of obese animals

compared to lean animals or a derivative, homolog, analog, chemical equivalent or mimetic thereof;

(ii) an mRNA or a protein encoded by a nucleic acid molecule which molecule is differentially expressed in liver tissue of fed animals compared to fasted animals or a derivative, homolog, analog, chemical equivalent or mimetic thereof;

(iii) a protein encoded by a nucleotide sequence substantially as set forth in SEQ ID NO:1 or a derivative, homolog or analog thereof or a sequence encoding an amino acid sequence having at least about 40% similarity to this sequence or a derivative, homolog, analog, chemical equivalent or mimetic of said protein;

(iv) a protein encoded by a nucleotide sequence substantially as set forth in SEQ ID NO:2 or a derivative, homolog or analog thereof or a sequence encoding an amino acid sequence having at least about 40% similarity to this sequence or a derivative, homolog, analog, chemical equivalent or mimetic of said protein;

(v) a protein encoded by a nucleotide sequence substantially as set forth in SEQ ID NO:3 or a derivative, homolog or analog thereof or a sequence encoding an amino acid sequence having at least about 40% similarity to this sequence or a derivative, homolog, analog, chemical equivalent or mimetic of said protein;

(vi) a protein encoded by a nucleotide sequence substantially as set forth in SEQ ID NO:4 or a derivative, homolog or analog thereof or a sequence encoding an amino acid sequence having at least about 40% similarity to this sequence or a derivative, homolog, analog, chemical equivalent or mimetic of said protein;

(vii) a protein encoded by a nucleotide sequence substantially as set forth in SEQ ID NO:5 or a derivative, homolog or analog thereof or a sequence encoding an amino acid sequence having at least about 40% similarity to this sequence or a derivative, homolog, analog, chemical equivalent or mimetic of said protein;

(viii) a protein encoded by a nucleic acid molecule capable of hybridizing to the nucleotide sequence as set forth in SEQ ID NO:1 or a derivative, homolog or analog thereof under low stringency conditions;

(ix) a protein encoded by a nucleic acid molecule capable of hybridizing to the nucleotide sequence as set forth in SEQ ID NO:2 or a derivative, homolog or analog thereof under low stringency conditions;

(x) a protein encoded by a nucleic acid molecule capable of hybridizing to the nucleotide sequence as set forth in SEQ ID NO:3 or a derivative, homolog or analog thereof under low stringency conditions;

(xi) a protein encoded by a nucleic acid molecule capable of hybridizing to the nucleotide sequence as set forth in SEQ ID NO:4 or a derivative, homolog or analog thereof under low stringency conditions;

(xii) a protein encoded by a nucleic acid molecule capable of hybridizing to the nucleotide sequence as set forth in SEQ ID NO:5 or a derivative, homolog or analog thereof under low stringency conditions;

(xiii) a protein as defined in any one of paragraphs (i) to (xii) in a homodimeric form; and

(xiv) a protein as defined in any one of paragraphs (i) to (xii) in a heterodimeric form.

The protein of the present invention is preferably in isolated form. By "isolated" is meant a protein having undergone at least one purification step and this is conveniently defined, for example, by a composition comprising at least about 10% subject protein, preferably at least about 20%, more preferably at least about 30%, still more preferably at least about 40-50%, even still more preferably at least about 60-70%, yet even still more preferably

80-90% or greater, such as 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 and 100% of subject protein relative to other components as determined by molecular weight, amino acid sequence or other convenient means. The protein of the present invention may also be considered, in a preferred embodiment, to be biologically pure.

The identification of *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203* permits the generation of a range of therapeutic molecules capable of modulating expression of *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203* or modulating the activity of AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203. Modulators contemplated by the present invention includes agonists and antagonists of AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 expression. Antagonists of *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203* expression include antisense molecules, ribozymes and co-suppression molecules. Agonists include molecules which increase promoter activity or which interfere with negative regulatory mechanisms. Antagonists of AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 include antibodies and inhibitor peptide fragments. All such molecules may first need to be modified to enable such molecules to penetrate cell membranes. Alternatively, viral agents may be employed to introduce genetic elements to modulate expression of *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203.*

The present invention contemplates, therefore, a method for modulating expression of one or more of *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203* in a mammal, said method comprising contacting the *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203* gene with an effective amount of a modulator of *AGT-106, AGT-113, AGT-201, AGT-202* and/or *AGT-203* expression for a time and under conditions sufficient to up-regulate or down-regulate or otherwise modulate expression of *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203.* For example, a nucleic acid molecule encoding *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203* or a derivative or homolog thereof may be introduced

into a cell to enhance the ability of that cell to produce AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203, conversely, *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203* antisense sequences such as oligonucleotides may be introduced to decrease the availability of AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 molecules.

Another aspect of the present invention contemplates a method of modulating activity of AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 in a mammal, said method comprising administering to said mammal a modulating effective amount of a molecule for a time and under conditions sufficient to increase or decrease AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 activity. The molecule may be a proteinaceous molecule or a chemical entity and may also be a derivative of AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 or its ligand.

Modulating levels of *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203* expression is important in the treatment of a range of conditions such as mitochondrial dysfunction, myopathy, genetic disorder or cancer. The present invention has application in the treatment of humans as well as in the veterinary and animal husbandry industries. Accordingly, subjects contemplated for treatment in accordance with the present invention includes, but is not limited to humans, primates, livestock animals (e.g. pigs, sheep, cows, horses, donkeys, camels), laboratory test animals (e.g. mice, rats, guinea pigs, hamsters, rabbits), companion animals (e.g. dogs, cats) and captured wild animals (e.g. foxes, kangaroos, deer). A particularly preferred host is a human, primate or livestock animal.

In a particularly preferred aspect of the invention down-regulation of AGT-203 is proposed to be useful in the treatment of cervical cancer whereas up-regulation of AGT-203 is proposed to be useful in cancers of the kidney, breast and pancreas.

Accordingly, the present invention contemplates therapeutic and prophylactic uses of AGT-106, AGT-113, AGT-201, AGT-202 and/or AGT-203 amino acid and nucleic acid molecules in addition to AGT-106, AGT-113, AGT-201, AGT-202 and/or AGT-203 agonistic and antagonistic agents.

The present invention contemplates, therefore, a method of modulating expression of AGT-106, AGT-113, AGT-201, AGT-202 and/or AGT-203 in a mammal, said method comprising contacting the *AGT-106, AGT-113, AGT-201, AGT-202* and/or *AGT-203* genes with an effective amount of an agent for a time and under conditions sufficient to up-regulate, down-regulate or otherwise module expression of *AGT-106, AGT-113, AGT-201, AGT-202* and/or *AGT-203*. For example, antisense sequences such as oligonucleotides may be utilized.

Conversely, nucleic acid molecules encoding AGT-106, AGT-113, AGT-201, AGT-202 and/or AGT-203 or derivatives thereof may be introduced to up-regulate one or more specific functional activities.

Another aspect of the present invention contemplates a method of modulating activity of AGT-106, AGT-113, AGT-201, AGT-202 and/or AGT-203 in a subject, said method comprising administering to said subject a modulating effective amount of an agent for a time and under conditions sufficient to increase or decrease AGT-106, AGT-113, AGT-201, AGT-202 and/or AGT-203 activity.

Modulation of activity by the administration of an agent to a mammal can be achieved by one of several techniques, including but in no way limited to introducing into said mammal a proteinaceous or non-proteinaceous molecule which:

(i) modulates expression of *AGT-106, AGT-113, AGT-201, AGT-202* and/or *AGT-203*;

(ii) functions as an antagonist of AGT-106, AGT-113, AGT-201, AGT-202 and/or AGT-203;

(iii) functions as an agonist of AGT-106, AGT-113, AGT-201, AGT-202 and/or AGT-203.

The proteinaceous molecule may be derived from natural or recombinant sources including fusion proteins or following, for example, natural product screening or the screening of chemical libraries. The non-proteinaceous molecule may be, for example, a nucleic acid molecule or may be derived from natural sources, such as for example natural product screening or may be chemically synthesized. The present invention contemplates chemical analogs of AGT-106, AGT-113, AGT-201, AGT-202 and/or AGT-203 or small molecules capable of acting as agonists or antagonists. Chemical agonists may not necessarily be derived from AGT-106, AGT-113, AGT-201, AGT-202 and/or AGT-203 but may share certain conformational similarities. Alternatively, chemical agonists may be specifically designed to mimic certain physiochemical properties. Antagonists may be any compound capable of blocking, inhibiting or otherwise preventing AGT-106, AGT-113, AGT-201, AGT-202 and/or AGT-203 from carrying out their normal biological functions. Antagonists include monoclonal antibodies, antisense and sense nucleic acids which prevent transcription or translation of *AGT-106, AGT-113, AGT-201, AGT-202* and/or *AGT-203* genes or mRNA in mammalian cells. Modulation of expression may also be achieved utilizing antigens, RNA, RNAi, ribosomes, DNAzymes, RNA aptamers or antibodies.

The proteinaceous or non-proteinaceous molecule may act either directly or indirectly to modulate the expression of *AGT-106, AGT-113, AGT-201, AGT-202* and/or *AGT-203* or the activity of AGT-106, *AGT-113*, AGT-201, AGT-202 and/or AGT-203. Said molecule acts directly if it associates with *AGT-106, AGT-113, AGT-201, AGT-202* and/or *AGT-203* or AGT-106, *AGT-113*, AGT-201, AGT-202 and/or AGT-203 to modulate expression or activity. Said molecule acts indirectly if it associates with a molecule other than *AGT-106, AGT-113, AGT-201, AGT-202* and/or *AGT-203* or AGT-106, *AGT-113*, AGT-201, AGT-202 and/or AGT-203 which other molecule either directly or indirectly modulates the expression or activity of *AGT-106, AGT-113, AGT-201, AGT-202* and/or *AGT-203* or AGT-106, AGT-113, AGT-201, AGT-202 and/or AGT-203. Accordingly, the method of the present invention encompasses the regulation of *AGT-106, AGT-113, AGT-201, AGT-202* and/or *AGT-203* or AGT-106, AGT-113, AGT-201, AGT-202 and/or AGT-203 expression or activity *via* the induction of a cascade of regulatory steps.

The molecules which may be administered to a mammal in accordance with the present invention may also be linked to a targeting means such as a monoclonal or polyclonal antibody, which provides specific delivery of these molecules to the target cells.

A further aspect of the present invention relates to the use of the invention in relation to mammalian disease conditions. For example, the present invention is particularly useful but in no way limited to use in a therapeutic or prophylactic treatment of mitochondrial dysfunction, myopathy, genetic disorder or cancer.

Accordingly, another aspect of the present invention relates to a method of treating a mammal suffering from a condition characterized by one or more symptoms of a mitochondrial dysfunction, myopathy, genetic disorder or cancer, said method comprising administering to said mammal an effective amount of an agent for a time and under conditions sufficient to modulate the expression of *AGT-106, AGT-113, AGT-201, AGT-202* and/or *AGT-203* or sufficient to modulate the activity of AGT-106, AGT-113, AGT-201, AGT-202 and/or AGT-203.

One particularly useful method of treatment is the modulation of levels of AGT-203. For example, down-regulation of AGT-203 is proposed in the treatment of cervical cancer and up-regulation of AGT-203 is proposed in the treatment of cancers of the kidney, breast and pancreas.

In another aspect, the present invention relates to a method of treating a mammal suffering from a disease condition characterized by one or more symptoms of mitochondrial dysfunction, myopathy, genetic disorder or cancer, said method comprising administering to said mammal an effective amount of AGT-106, AGT-113, AGT-201, AGT-202 and/or AGT-203 or *AGT-106, AGT-113, AGT-201, AGT-202* and/or *AGT-203*.

As used herein "myopathy" refers to any abnormal conditions or disease of the muscle tissues, which include the muscles over our bones (skeletal muscle) and the heart (cardiac muscle).

Mitochondrial dysfunction relates to abnormalities in mitochondria. Mitochondria are part of the cell (organelle) that is responsible for energy production. The organelle consists of two sets of membranes, a smooth continuous outer coat and an inner membrane arranged in tubules or in folds that form plate-like double membranes (cristae). Mitochondria are the principal energy source of the cell, containing the cytochrome enzymes of terminal electron transport and the enzymes of the citric acid cycle, fatty acid oxidation, and oxidative phosphorylation. They are responsible for converting nutrients into energy as well as many other specialized tasks. Mitochondria are complex organelles located in virtually all cells of the body. A large degree of their complexity is due to the fact that over 1000 proteins are located in the mitochondria. Thirteen of these proteins are encoded by the mitochondrial DNA (mtDNA), while the remainder are nuclear-encoded, and imported into the mitochondria.

Symptoms of mitochondrial dysfunction include weakness (which may be intermittent), neuropathic pain, absent reflexes, gastrointestinal problem (gastroesophogeal reflux, delayed gastric emptying, constipation, pseudo-obstruction), fainting, absent or excessive sweating resulting in temperature regulation problems, hypotonia, cramping and muscle pain, proximal renal tubular wasting resulting in loss of protein, magnesium, phosphorous, calcium and other electrolytes, cardiac conduction defects (heart blocks) and cardiomyopathy, hypoglycemia (low blood sugar) and liver failure, visual loss and blindness, hearing loss and deafness, and diabetes and exocrine pancreatic failure (inability to make digestive enzymes).

There may also be systemic problems associated with mitochondrial dysfunction, including failure to gain weight, short stature, fatigue, respiratory problems.

Mitochondrial defects have been linked to Alzheimer's, Parkinson's, diabetes, autism, and the aging process. Other disease associated with mitochondrial dysfunction include, LIC (Lethal Infantile Cardiomyopathy), Beta-oxidation Defects, COX Deficiency, Mitochondrial Cytopathy, Alpers Disease, Barth syndrome, Carnitine-Acyl-Carnitine Deficiency, Carnitine Deficiency, Co-Enzyme Q10 Deficiency, Complex I Deficiency, Complex II Deficiency, Complex III Deficiency, Complex IV Deficiency, Complex V Deficiency, CPEO, CPT I Deficiency, Glutaric Aciduria Type II, KSS, lactic acidosis, LCAD, LCHAD, Leigh Disease, LHON, Luft Disease, MAD, MCA, MELAS, MERRF, mitochondrial DNA depletion, Mitochondrial Encephalopathy, MNGIE, NARP, Pearson Syndrome, Pyruvate Carboxylase Deficiency, Pyruvate Dehydrogenase Deficiency, SCAD, SCHAD and VLCAD.

Alpers Disease, or Progressive Infantile Poliodystrophy, includes symptoms such as seizures, dementia, spasticity, blindness, liver dysfunction, and cerebral degeneration. (Luft; The development of mitochondrial medicine. *Proceedings of the National Academy of Sciences of the United States of America*; 1994; 91(19); 8731-8).

Barth syndrome or LIC (Lethal Infantile Cardiomyopathy) is an X-linked recessive disorder the symptoms of which include skeletal myopathy, cardiomyopathy, short stature, and neutropenia. (Christodoulou; Barth Syndrome: Clinical Observations and Genetic Linkage Studies. *American Journal of Medical Genetics*; *50(3)*:255-64, 1994).

Carnitine-Acyl-Carnitine Deficiency is an autosomal recessive disorder, the symptoms of which are seizures, apnea, bradycardia, vomiting, lethargy, coma, enlarged liver, limb weakness, myoglobin in the urine, Reye-like symptoms triggered by fasting.

Carnitine Deficiency is an autosomal recessive disease, the symptoms of which include Cardiomyopathy, failure to thrive, and altered consciousness or coma, sometimes hypotonia.

Co-Enzyme Q10 Deficiency is most likely an autosomal recessive disease, the symptoms of which include Encephalomyopathy, mental retardation, exercise intolerance, ragged-red fibers, and recurrent myoglobin in the urine.

Complex I Deficiency or NADH dehydrogenase (NADH-CoQ reductase) deficiency is an autosomal disease, the symptoms of which are classified by three major forms: (1) fatal infantile multisystem disorder, characterized by developmental delay, muscle weakness, heart disease, congenital lactic acidosis, and respiratory failure; (2) myopathy beginning in childhood or in adult life, manifesting as exercise intolerance or weakness. Elevated lactic acid common; and (3) mitochondrial encephalomyopathy (including MELAS), which may begin in childhood or adult life and consists of variable combinations of symptoms and signs, including ophthalmoplegia, seizures, dementia, ataxia, hearing loss, pigmentary retinopathy, sensory neuropathy, and uncontrollable movements. In addition, this disorder may cause Leigh Syndrome.

Complex II Deficiency or Succinate dehydrogenase deficiency, the symptoms of which include encephalomyopathy and various manifestations, including failure to thrive, developmental delay, hyoptonia, lethargy, respiratory failure, ataxia, myoclonus and lactic acidosis. May also cause Leigh Syndrome.

Complex III Deficiency or Ubiquinone-cytochrome c oxidoreductase deficiency, symptoms of which are categorized in four major forms: (1) fatal infantile encephalomyopathy, congenital lactic acidosis, hypotonia, dystrophic posturing, seizures, and coma. Ragged-red fibers common; (2) encephalomyopathies of later onset (childhood to adult life): various combinations of weakness, short stature, ataxia, dementia, hearing loss, sensory neuropathy, pigmentary retinopathy, and pyramidal signs. Ragged-red fibers common. Possible lactic acidosis; (3) myopathy, with exercise intolerance evolving into fixed weakness. Ragged-red fibers common. Possible lactic acidosis; and (4) infantile histiocytoid cardiomyopathy.

Complex IV Deficiency or Cytochrome c oxidase deficiency is caused by a defect in Complex IV of the respiratory chain, the symptoms of which can be categorized in two major forms: (1) encephalomyopathy, which is typically normal for the first 6 to 12 months of life and then show developmental regression, ataxia, lactic acidosis, optic atrophy, ophthalmoplegia, nystagmus, dystonia, pyramidal signs, respiratory problems and frequent seizures; and (2) myopathy: Two main variants: (a) Fatal infantile myopathy: may begin soon after birth and accompanied by hypotonia, weakness, lactic acidosis, ragged-red fibers, respiratory failure, and kidney problems: and (b) Benign infantile myopathy: may begin soon after birth and accompanied by hypotonia, weakness, lactic acidosis, ragged-red fibers, respiratory problems, but (if the child survives) followed by spontaneous improvement.

Complex V Deficiency or ATP synthase deficiency includes symptoms such as slow, progressive myopathy.

CPEO or Chronic Progressive External Ophthalmoplegia Syndrome includes symptoms such as visual myopathy, retinitis pigmentosa, dysfunction of the central nervous system. It is caused by single mitochondrial DNA deletions, with Mitochondrial DNA point mutation, A3243G being the most common (Luft; The development of mitochondrial medicine. [Review]; *Proceedings of the National Academy of Sciences of the United States of America*;1994 ;91(19); 8731-8).

CPT I Deficiency is an autosomal recessive disease and includes symptoms such as enlarged liver and recurrent Reye-like episodes triggered by fasting or illnesses.

CPT II Deficiency is an autosomal recessive disease, the symptoms of which include exercise intolerance, fasting intolerance, muscle pain, muscle stiffness, and myoglobin in the urine and in infants, Reye-like syndrome, enlarged liver, hypoglycemia, enlarged heart and cardiac arrhythmia.

KSS or Kearns-Sayre Syndrome, in most cases is caused by large mitochondria DNA deletions. Symptoms associated with KSS include progressive external ophthalmoplegia, pigmentary retinopathy, heart block, and high cerebrospinal protein.

Lactic Acidosis is associated with the accumulation of lactic acid due to its production exceeding its use. Chronic lactic acidosis is a common symptom of mitochondrial disease.

LCAD or Long-Chain Acyl-CoA Dehydrogenase Deficiency, is an autosomal recessive disorder, which causes a fatal syndrome, in infants, typified by failure to thrive, enlarged liver, enlarged heart, metabolic encephalopathy and hypotonia.

LCHAD is an autosomal recessive disorder, characterized by symptoms such as encephalopathy, liver dysfunction, cardiomyopathy, and myopathy. Also pigmentary retinopathy and peripheral neuropathy.

Leigh Disease or Syndrome or Subacute Necrotizing Encephalomyelopathy is characterized by symptoms such as Seizures, hypotonia, fatigue, nystagmus, poor reflexes, eating and swallowing difficulties, breathing problems and poor motor function.

LHON or Leber Hereditary Optic Neuropathy is caused by mitochondrial DNA point mutations, including G14459A, among others. Symptoms associated with LHON include primarily blindness in young men. Less common symptoms include mild dementia, ataxia, spasticity, peripheral neuropathy and heart conduction defects.

Luft Disease is characterized by symptoms such as hypermetabolism, with fever, heat intolerance, profuse perspiration, polyphagia, polydipsia, ragged-red fibers, and resting tachycardia. In addition to exercise intolerance with mild weakness.

MAD or Glutaric Aciduria Type II or multiple Acyl-CoA Dehydrogenase Deficiency is caused by defects of the flavoproteins responsible for transferring electrons (ETF or ETF-

dehydrogenase) therefore affecting the function of all six ETF-funneling acyl-CoA dehydrogenases

MCAD or Medium-Chain Acyl-CoA Dehydrogenase Deficiency is an autosomal recessive disorder, which afflicts infants or young children with episodes of encephalopathy, enlarged and fatty degeneration of the liver, and low carnitine in the blood.

MELAS or Mitochondrial Encephalomyopathy Lactic Acidosis and Strokelike Episodes is caused by mitochondrial DNA point mutations, the most common of which is A3243G. It is characterized by symptoms: Short stature, seizures, stroke-like episodes with focused neurological deficits, recurrent headaches, cognitive regression, disease progression ragged-red fibers (Koo, *et. al.*; Mitochondrial encephalomyopathy, lactic acidosis, stroke-like episodes (MELAS): clinical, radiological, pathological, and genetic observations; *Annals of Neurology*; *34(1)*:25-32, 1993).

MERRF or Myoclonic Epilepsy and Ragged-Red Fiber Disease is caused by the mitochondrial DNA point mutations A8344G and T8356C. Its symptoms include myoclonus, epilepsy, progressive ataxia, muscle weakness and degeneration, deafness and dementia (Luft; *Proceedings of the National Academy of Sciences of the United States of America*; *91(19)*:8731-8, 1994).

There are three forms of mitochondrial DNA Depletion. These include: (1) congenital myopathy: Neonatal weakness, hypotonia requiring assisted ventilation, possible renal dysfunction. Severe lactic acidosis. Prominent ragged-red fibers. Death due to respiratory failure usually occurs prior to one year of age; (2) infantile myopathy: Following normal early development until one year old, weakness appears and worsens rapidly, causing respiratory failure and death typically within a few years; and (3) hepatopathy, enlarged liver and intractable liver failure, myopathy. Severe lactic acidosis. Death is typical within the first year.

Mitochondrial Encephalopathy also includes Encephalomyopathy and Encephalomyelopathy.

MNGIE or Myoneurogastrointestinal Disorder and Encephalopathy, include symptoms such as progressive external ophthalmoplegia, limb weakness, peripheral neuropathy, digestive tract disorders, leukodystrophy, lactic acidosis and ragged red fibers.

NARP or Neuropathy, Ataxia, and Retinitis Pigmentosa is caused by mitochondrial DNA point mutations in genes associated with Complex V, including T8993G, (also T8993C by some researchers). Leigh Syndrome may result if the percentage of mutation is high enough.

Pearson Syndrome is characterized by symptoms associated with bone marrow and pancreas dysfunction. It is caused by single mitochondrial DNA deletions. Inheritance is usually sporadic. Those who survive infancy usually develop Kearns-Sayre Syndrome.

Pyruvate Carboxylase Deficiency is an autosomal recessive disorder, the symptoms of which include lactic acidosis, hypoglycemia, severe retardation, failure to thrive, in addition to seizures and spasticity.

Pyruvate Dehydrogenase Deficiency is characterized by symptoms such as lactic acidosis, ataxia, pyruvic acidosis, spinal and cerebellar degeneration. Less common symptoms include agenesis of the corpus callosum and lesions in the basal ganglia, cerebellum, and brain stem, growth delay, hypotonia, seizures and polyneuropathy.

SCAD or Short-Chain Acyl-CoA Dehydrogenase Deficiency, is an autosomal recessive disorder characterized by symptoms such as failure to thrive, developmental delay and hypoglycemia.

SCHAD is an autosomal recessive disorder, characterized by encephalopathy and possibly liver disease or cardiomyopathy.

VLCAD or Very Long-Chain Acyl-CoA Dehydrogenase Deficiency is an autosomal recessive disorder, characterized by various manifestations, ranging from fatal infantile encephalopathy to recurrent myoglobin in the urine, similar to the myopathic form of CPT II deficiency.

In addition, other diseases and disorders which can be treated using the methods of the present invention include, without being limited to, A-Beta-Lipoproteinemia, A-V, A Beta-2-Microglobulin Amyloidosis, A-T, A1AD, A1AT, Aagenaes, Aarskog syndrome, Aarskog-Scott Syndrome, Aase-smith syndrome, Aase Syndrome, AAT, Abderhalden-Kaufmann-Lignac Syndrome, Abdominal Muscle Deficiency Syndrome, Abdominal Wall Defect, Abdominal Epilepsy, Abdominal Migraine, Abductor Spasmodic Dysphonia, Abductor Spastic Dysphonia, Abercrombie Syndrome, blepharon-Macrostomia Syndrome, ABS, Absence of HPRT, Absence of Corpus Callosum Schinzel Typ, Absence Defect of Limbs Scalp and Skull, Absence of Menstruation Primar, Absence of HGPRT, Absorptive Hyperoxaluriaor Enteric, Abt-Letterer-Siwe Disease, ACADL, ACADM Deficiency, ACADM, ACADS, Acanthocytosis-Neurologic Disorder, Acanthocytosis, Acantholysis Bullosa, Acanthosis Nigricans, Acanthosis Bullosa, Acanthosis Nigricans With Insulin Resistance Type A, Acanthosis Nigricans With Insulin Resistance Type B, Acanthotic Nevus, Acatalasemia, Acatalasia, ACC, Accessory Atrioventricular Pathways, Accessory Atrioventricular Pathways, Acephaly, ACF with Cardiac Defects, Achalasia, Achard-Thiers Syndrome, ACHARD (Marfan variant), Achard's syndrome, Acholuric Jaundice, Achondrogenesis, Achondrogenesis Type IV, Achondrogenesis Type III, Achondroplasia, Achondroplasia Tarda, Achondroplastic Dwarfism, Achoo Syndrome, Achromat, Achromatope, Achromatopic, Achromatopsia, Achromic Nevi, Acid Ceramidase Deficiency, Acid Maltase Deficiency, Acid Beta-glucosidase Deficiency, Acidemia Methylmalonic, Acidemia Propionic, Acidemia with Episodic Ataxia and Weakness, Acidosis, Aclasis Tarsoepiphyseal, ACM, Acoustic Neurilemoma, Acoustic Neuroma, ACPS with Leg Hypoplasia, ACPS II, ACPS IV, ACPS III, Acquired Aphasia with Convulsive Disorder, Acquired Brown Syndrome, Acquired Epileptic Aphasia, Acquired Factor XIII Deficiency, Acquired Form of ACC (caused by infection while still in womb),

Acquired Hyperoxaluria, Acquired Hypogammaglobulinemia, Acquired Immunodeficiency Syndrome (AIDS), Acquired Iron Overload, Acquired Lipodystrophy, Acquired Partial Lipodystrophy, Acquired Wandering Spleen, ACR, Acral Dysostosis with Facial and Genital Abnormalities, Acro Renal, Acrocallosal Syndrome Schinzel Type, Acrocephalosyndactyly, Acrocephalosyndactyly Type I, Acrocephalosyndactyly Type I Subtype I, Acrocephalopolysyndactyly Type II, Acrocephalopolysyndactyly Type III, Acrocephalopolysyndactyly Type IV, Acrocephalosyndactyly V (ACS5 or ACS V) Subtype I, Acrocephaly Skull Asymmetry and Mild Syndactyly, Acrocephaly, Acrochondrohyperplasia, Acrodermatitis Enteropathica, Acrodysostosis, Acrodystrophic Neuropathy, Acrofacial Dysostosis Nager Type, Acrofacial Dysostosis Postaxial Type, Acrofacial Dysostosis Type Genee-Wiedep, Acrogeria Familial, Acromegaly, Acromelalgia Hereditary, Acromesomelic Dysplasia, Acromesomelic Dwarfism, Acromicric Skeletal Dysplasia, Acromicric Dysplasia, Acroosteolysis with Osteoporosis and Changes in Skull and Mandible, Acroosteolysis, Acroparesthesia, ACS I, ACS Type III, ACS, ACS3, ACTH Deficiency, Action Myoclonus, Acute Brachial Neuritis Syndrome, Acute Brachial Radiculitis Syndrome, Acute Cerebral Gaucher Disease, Acute Cholangitis, Acute Disseminated Encephalomyeloradiculopathy, Acute Disseminated Histiocytosis-X, Acute Hemorrhagic Polioencephalitis, Acute Idiopathic Polyneuritis, Acute Immune-Mediation Polyneuritis, Acute Infantile Pelizaeus-Merzbacher Brain Sclerosis, Acute Intermittant Porphyria, Acute Porphyrias, Acute Sarcoidosis, Acute Shoulder Neuritis, Acute Toxic Epidermolysis, Acyl-CoA Dehydrogenase Deficiency Long-Chain, Acyl-CoA Dehydrogenase Deficiency Short-Chain, Acyl-CoA Dihydroxyacetone Acyltransferase, Acyl-coenzyme A Oxidase Deficiency, ADA, ADA Deficiency, Adam Complex, Adamantiades-Behcet's Syndrome, Adamantinoma, Adams Oliver Syndrome, Adaptive Colitis, ADD combined type, ADD, Addison Disease with Cerebral Sclerosis, Addison's Anemia, Addison's Disease, Addison-Biermer Anemia, Addison-Schilder Disease, Addisonian Pernicious Anemia, Adducted Thumbs-Mental Retardation, Adductor Spasmodic Dysphonia, Adductor Spastic Dysphonia, Adenoma Associated Virilism of Older Women, Adenomatosis of the Colon and Rectum, Adenomatous polyposis of the Colon, Adenomatous Polyposis Familial, Adenosine Deaminase Deficiency, Adenylosuccinase deficiency, ADHD predominantly hyperactive-

impulsive type, ADHD predominantly inattentive type, ADHD, Adhesive Arachnoiditis, Adie Syndrome, Adie's Syndrome, Adie's Tonic Pupil, Adie's Pupil, Adipogenital Retinitis Pigmentosa Polydactyly, Adipogenital-Retinitis Pigmentosa Syndrome, Adiposa Dolorosa, Adiposis Dolorosa, Adiposogenital Dystrophy, Adolescent Cystinosis, ADPKD, Adrenal Cortex Adenoma, Adrenal Disease, Adrenal Hyperfunction resulting from Pituitary ACTH Excess, Adrenal Hypoplasia, Adrenal Insufficiency, Adrenal Neoplasm, Adrenal Virilism, Adreno-Retinitis Pigmentosa-Polydactyly Syndrome, Adrenocortical Insufficiency, Adrenocortical Hypofunction, Adrenocorticotropic Hormone Deficiency Isolated, Adrenogenital Syndrome, Adrenoleukodystrophy, Adrenomyeloneuropathy, Adreno-Retinitis Pigmentosa-Polydactyly Syndrome, Adult Cystinosis, Adult Dermatomyositis, Adult Hypophosphatasia, Adult Macula Lutea Retinae Degeneration, Adult Onset ALD, Adult-Onset Ceroidosis, Adult Onset Medullary Cystic Disease, Adult Onset Pernicious Anemia, Adult Onset Pernicious Anemia, Adult Onset Schindler Disease, Adult-Onset Subacute Necrotizing Encephalomyelopathy, Adult Polycystic Kidney Disease, Adult Onset Medullary Cystic Disease, Adynlosuccinate Lyase Deficiency, AE, AEC Syndrome, AFD, Afibrinogenemia, African Siderosis, AGA, Aganglionic Megacolon, Age Related Macular Degeneration, Agenesis of Commissura Magna Cerebri, Agenesis of Corpus Callosum, Agenesis of Corpus Callosum-Infantile Spasms-Ocular Anomalies, Agenesis of Corpus Callosum and Chorioretinal Abnormality, Agenesis of Corpus Callosum-Chorioretinitis Abnormality, Aggressive mastocytosis, Agnosis Primary, AGR Triad, AGU, Agyria, Agyria-pachygria-band spectrum, AHC, AHD, AHDS, AHF Deficiency, AHG Deficiency, AHO, Ahumada Del Castillo, Aicardi Syndrome, AIED, AIMP, AIP, AIS, Akinetic Seizure, ALA-D Porphyria, Alactasia, Alagille Syndrome, Aland Island Eye Disease (X-Linked), Alaninuria, Albers-Schonberg Disease, Albinism, Albinismus, Albinoidism, Albright Hereditary Osteodystrophy, Alcaptonuria, Alcohol-Related Birth Defects, Alcoholic Embryopathy, Ald, ALD, Aldosterone, Aldosteronism With Normal Blood Pressure, Aldrich Syndrome, Alexander's Disease, Alexanders Disease, Algodystrophy, Algoneurodystrophy, Alkaptonuria, Alkaptonuric Ochronosis, Alkyl DHAP synthase deficiency, Allan-Herndon-Dudley Syndrome, Allan-Herndon Syndrome, Allan-Herndon-Dudley Mental Retardation, Allergic Granulomatous Angiitis, Allergic Granulomatous Angiitis of Cronkhite-Canada, Alobar Holoprosencephaly,

Alopecia Areata, Alopecia Celsi, Alopecia Cicatrisata, Alopecia Circumscripta, Alopecia-Poliosis-Uveitis-Vitiligo-Deafness-Cutaneous-Uveo-O, Alopecia Seminuniversalis, Alopecia Totalis, Alopecia Universalis, Alpers Disease, Alpers Diffuse Degeneration of Cerebral Gray Matter with Hepatic Cirrhosis, Alpers Progressive Infantile Poliodystrophy, Alpha-1-Antitrypsin Deficiency, Alpha-1 4 Glucosidase Deficiency, Alpha-Galactosidase A Deficiency, Alpha-Galactosidase B Deficiency, Alpha High-Density Lipoprotein Deficiency, Alpha-L-Fucosidase Deficiency Fucosidosis Type 3, Alpha-GalNAc Deficiency Schindler Type, Alpha-L-Fucosidase Deficiency Fucosidosis Type 3, Alphalipoproteinemia, Alpha Mannosidosis, Alpha-N-Acetylgalactosaminidase Deficiency Schindler Type, Alpha-NAGA Deficiency Schindler Type, Alpha-Neuraminidase Deficiency, Alpha-Thalassemia/mental retardation syndrome non-deletion type, Alport Syndrome, ALS, Alstroem's Syndrome, Alstroem, Alstrom Syndrome, Alternating Hemiplegia Syndrome, Alternating Hemiplegia of Childhood, Alzheimer's Disease, Amaurotic Familial Idiocy, Amaurotic Familial Idiocy Adult, Amaurotic Familial Infantile Idiocy, Ambiguous Genitalia, AMC, AMD, Ameloblastoma, Amelogenesis Imperfecta, Amenorrhea-Galactorrhea Nonpuerperal, Amenorrhea-Galactorrhea-FSH Decrease Syndrome, Amenorrhea, Amino Acid Disorders, Aminoaciduria-Osteomalacia-Hyperphosphaturia Syndrome, AMN, Amniocentesis, Amniotic Bands, Amniotic Band Syndrome, Amniotic Band Disruption Complex, Amniotic Band Sequence, Amniotic Rupture Sequence, Amputation Congenital, AMS, Amsterdam Dwarf Syndrome de Lange, Amylo-1 6-Glucosidase Deficiency, Amyloid Arthropathy of Chronic Hemodialysis, Amyloid Corneal Dystrophy, Amyloid Polyneuropathy, Amyloidosis, Amyloidosis of Familial Mediterranean Fever, Amylopectinosis, Amyoplasia Congenita, Amyotrophic Lateral Sclerosis, Amyotrophic Lateral Sclerosis, Amyotrophic Lateral Sclerosis-Polyglucosan Bodies, AN, AN 1, AN 2, Anal Atresia, Anal Membrane, Anal Rectal Malformations, Anal Stenosis, Analine 60 Amyloidosis, Analphalipoproteinemia, Analrectal, Anaplastic Astrocytoma, Andersen Disease, Anderson-Fabry Disease, Andersen Glycogenosis, Anderson-Warburg Syndrome, Andre Syndrome, Andre Syndrome Type II, Androgen Insensitivity, Androgen Insensitivity Syndrome Partial, Androgen Insensitivity Syndrome, Androgen Insensitivity Syndrome Partial, Androgenic Steroids, Anemia Autoimmune Hemolytic, Anemia Blackfan Diamond, Anemia,

Congenital, Triphalangeal Thumb Syndrome, Anemia Hemolytic Cold Antibody, Anemia Hemolytic with PGK Deficiency, Anemia Pernicious, Anencephaly, Angelman Syndrome, Angio-Osteohypertrophy Syndrome, Angiofollicular Lymph Node Hyperplasia, Angiohemophilia, Angiokeratoma Corporis, Angiokeratoma Corporis Diffusum, Angiokeratoma Diffuse, Angiomatosis Retina, Angiomatous Lymphoid, Angioneurotic Edema Hereditary, Anhidrotic Ectodermal Dysplasia, Anhidrotic X-Linked Ectodermal Dysplasias, Aniridia, Aniridia-Ambiguous Genitalia-Mental Retardation, Aniridia Associated with Mental Retardation, Aniridia-Cerebellar Ataxia-Mental Deficiency, Aniridia Partial-Cerebellar Ataxia-Mental Retardation, Aniridia Partial-Cerebellar Ataxia-Oligophrenia, Aniridia Type I, Aniridia Type II, Aniridia-Wilms' Tumor Association, Aniridia-Wilms' Tumor-Gonadoblastoma, Ankyloblepharon-Ectodermal Defects-Cleft Lip/Palate, Ankylosing Spondylitis, Annular groves, Anodontia, Anodontia Vera, Anomalous Trichromasy, Anomalous Dysplasia of Dentin, Coronal Dentin Dysplasia, Anomic Aphasia, Anophthalmia, Anorectal, Anorectal Malformations, Anosmia, Anterior Bowing of the Legs with Dwarfism, Anterior Membrane Corneal Dystrophy, Anti-Convulsant Syndrome, Anti-Epstein-Barr Virus Nuclear Antigen (EBNA) Antibody Deficiency, Antibody Deficiency, Antibody Deficiency with near normal Immunoglobulins, Antihemophilic Factor Deficiency, Antihemophilic Globulin Deficiency, Antiphospholipid Syndrome, Antiphospholipid Antibody Syndrome, Antithrombin III Deficiency, Antithrombin III Deficiency Classical (Type I), Antitrypsin Deficiency, Antley-Bixler Syndrome, Antoni's Palsy, Anxietas Tibialis, Aorta Arch Syndrome, Aortic and Mitral Atresia with Hypoplasic Left Heart Syndrome, Aortic Stenosis, Aparoschisis, APC, APECED Syndrome, Apert Syndrome, Aperts, Aphasia, Aplasia Axialis Extracorticales Congenital, Aplasia Cutis Congenita, Aplasia Cutis Congenita with Terminal Transverse Limb Defects, Aplastic Anemia, Aplastic Anemia with Congenital Anomalies, APLS, Apnea, Appalachian Type Amyloidosis, Apple Peel Syndrome, Apraxia, Apraxia Buccofacial, Apraxia Constructional, Apraxia Ideational, Apraxia Ideokinetic, Apraxia Ideomotor, Apraxia Motor, Apraxia Oculomotor, APS, Arachnitis, Arachnodactyly Contractural Beals Type, Arachnodactyly, Arachnoid Cysts, Arachnoiditis Ossificans, Arachnoiditis, Aran-Duchenne, Aran-Duchenne Muscular Atrophy, Aregenerative Anemia, Arginase Deficiency, Argininemia, Arginino Succinase

Deficiency, Argininosuccinase Deficiency, Argininosuccinate Lyase Deficiency, Argininosuccinic Acid Lyase-ASL, Argininosuccinic Acid Synthetase Deficiency, Argininosuccinic Aciduria, Argonz-Del Castillo Syndrome, Arhinencephaly, Armenian Syndrome, Arnold-Chiari Malformation, Arnold-Chiari Syndrome, ARPKD, Arrhythmic Myoclonus, Arrhythmogenic Right Ventricular Dysplasia, Arteriohepatic Dysplasia, Arteriovenous Malformation, Arteriovenous Malformation, Arteriovenous Malformation of the Brain, Arteritis Giant Cell, Arthritis, Arthritis Urethritica, Arthro-Dento-Osteodysplasia, Arthro-Ophthalmopathy, Arthrochalasis Multiplex Congenita, Arthrogryposis Multiplex Congenita, Arthrogryposis Multiplex Congenita, Distal, Type IIA, ARVD, Arylsulfatase-B Deficiency, AS, ASA Deficiency, Ascending Paralysis, ASD, Atrioseptal Defects, ASH, Ashermans Syndrome, Ashkenazi Type Amyloidosis, ASL Deficiency, Aspartylglucosaminuria, Asperger's Syndrome, Asperger's Type Autism, Asphyxiating Thoracic Dysplasia, Asplenia Syndrome, ASS Deficiency, Asthma, Astrocytoma Grade I (Benign), Astrocytoma Grade II (Benign), Asymmetric Crying Facies with Cardiac Defects, Asymmetrical septal hypertrophy, Asymptomatic Callosal Agenesis, AT, AT III Deficiency, AT III Variant IA, AT III Variant Ib, AT 3, Ataxia, Ataxia Telangiectasia, Ataxia with Lactic Acidosis Type II, Ataxia Cerebral Palsy, Ataxiadynamia, Ataxiophemia, ATD, Athetoid Cerebral Palsy, Atopic Eczema, Atresia of Esophagus with or without Tracheoesophageal Fistula, Atrial Septal Defects, Atrial Septal Defect Primum, Atrial and Septal and Small Ventricular Septal Defect, Atrial Flutter, Atrial Fibrillation, Atriodigital Dysplasia, Atrioseptal Defects, Atrioventricular Block, Atrioventricular Canal Defect, Atrioventricular Septal Defect, Atrophia Bulborum Hereditaria, Atrophic Beriberi, Atrophy Olivopontocerebellar, Attention Deficit Disorder, Attention Deficit Hyperactivity Disorder, Attenuated Adenomatous Polyposis Coli, Atypical Amyloidosis, Atypical Hyperphenylalaninemia, Atypical Hyperphenylalaninemia, Auditory Canal Atresia, Auriculotemporal Syndrome, Autism, Autism Asperger's Type, Autism Dementia Ataxia and Loss of Purposeful Hand Use, Autism Infantile Autism, Autoimmune Addison's Disease, Autoimmune Hemolytic Anemia, Autoimmune Hepatitis, Autoimmune-Polyendocrinopathy-Candidias, Autoimmune Polyglandular Disease Type I, Autosomal Dominant Albinism, Autosomal Dominant Compelling Helioophthalmic Outburst Syndrome, Autosomal Dominant Desmin

Distal Myopathy with Late Onset, Autosomal Dominant EDS, Autosomal Dominant Emery-Dreifuss Muscular Dystrophy, Autosomal Dominant Keratoconus, Autosomal Dominant Pelizaeus-Merzbacher Brain Sclerosis, Autosomal Dominant Polycystic Kidney Disease, Autosomal Dominant Spinocerebellar Degeneration, Autosomal Recessive Agammaglobulinemia, Autosomal Recessive Centronuclear Myopathy, Autosomal Recessive Conradi-Hunermann Syndrome, Autosomal Recessive EDS, Autosomal Recessive Emery-Dreifuss Muscular Dystrophy, Autosomal Recessive Forms of Ocular Albinism, Autosomal Recessive Inheritance Agenesis of Corpus Callosum, Autosomal Recessive Keratoconus, Autosomal Recessive Polycystic Kidney Disease, Autosomal Recessive Severe Combined Immunodeficiency, AV, AVM, AVSD, AWTA, Axilla Abscess, Axonal Neuropathy Giant, Azorean Neurologic Disease, B-K Mole Syndrome, Babinski-Froelich Syndrome, BADS, Baillarger's Syndrome, Balkan Disease, Baller-Gerold Syndrome, Ballooning Mitral Valve, Balo Disease Concentric Sclerosis, Baltic Myoclonus Epilepsy, Bannayan-Zonana syndrome (BZS), Bannayan-Riley-Ruvalcaba syndrome, Banti's Disease, Bardet-Biedl Syndrome, Bare Lymphocyte Syndrome, Barlow's syndrome, Barraquer-Simons Disease, Barrett Esophagus, Barrett Ulcer, Barth Syndrome, Bartter's Syndrome, Basal Cell Nevus Syndrome, Basedow Disease, Bassen-Kornzweig Syndrome, Batten Disease, Batten-Mayou Syndrome, Batten-Spielmeyer-Vogt's Disease, Batten Turner Syndrome, Batten Turner Type Congenital Myopathy, Batten-Vogt Syndrome, BBB Syndrome, BBB Syndrome (Opitz), BBB Syndrome, BBBG Syndrome, BCKD Deficiency, BD, BDLS, BE, Beals Syndrome, Beals-Hecht Syndrome, Bean Syndrome, BEB, Bechterew Syndrome, Becker Disease, Becker Muscular Dystrophy, Becker Nevus, Beckwith Wiedemann Syndrome, Beckwith-Syndrome, Begnez-Cesar's Syndrome, Behcet's syndrome, Behcet's Disease, Behr 1, Behr 2, Bell's Palsy, Benign Acanthosis Nigricans, Benign Astrocytoma, Benign Cranial Nerve Tumors, Benign Cystinosis, Benign Essential Blepharospasm, Benign Essential Tremor, Benign Familial Hematuria, Benign Focal Amyotrophy, Benign Focal Amyotrophy of ALS, Benign Hydrocephalus, Benign Hypermobility Syndrome, Benign Keratosis Nigricans, Benign Paroxysmal Peritonitis, Benign Recurrent Hematuria, Benign Recurrent Intrahepatic Cholestasis, Benign Spinal Muscular Atrophy with Hypertrophy of the Calves, Benign Symmetrical Lipomatosis, Benign Tumors of the Central Nervous System,

Berardinelli-Seip Syndrome, Berger's Disease, Beriberi, Berman Syndrome, Bernard-Horner Syndrome, Bernard-Soulier Syndrome, Besnier Prurigo, Best Disease, Beta-Alanine-Pyruvate Aminotransferase, Beta-Galactosidase Deficiency Morquio Syndrome, Beta-Glucuronidase Deficiency, Beta Oxidation Defects, Beta-oxidation Defects, Beta Thalassemia Major, Beta Thalassemia Minor, Betalipoprotein Deficiency, Bethlem myopathy, Beuren Syndrome, BH4 Deficiency, Biber-Haab-Dimmer Corneal Dystrophy, Bicuspid Aortic Valve, Biedl-Bardet, Bifid Cranium, Bifunctional Enzyme Deficiency, Bilateral Acoustic Neurofibromatosis, Bilateral Acoustic Neuroma, Bilateral Right-Sidedness Sequence, Bilateral Renal Agenesis, Bilateral Temporal Lobe Disorder, Bilious Attacks, Bilirubin Glucuronosyltransferase Deficiency Type I, Binder Syndrome, Binswanger's Disease, Binswanger's Encephalopathy, Biotinidase deficiency, Bird-Headed Dwarfism Seckel Type, Birth Defects, Birthmark, Bitemporal Forceps Marks Syndrome, Biventricular Fibrosis, Bjornstad Syndrome, B-K Mole Syndrome, Black Locks-Albinism-Deafness of Sensoneural Type (BADS), Blackfan-Diamond Anemia, Blennorrheal Idiopathic Arthritis, Blepharophimosis, Ptosis, Epicanthus Inversus Syndrome, Blepharospasm, Blepharospasm Benign Essential, Blepharospasm Oromandibular Dystonia, Blessig Cysts, BLFS, Blindness, Bloch-Siemens Incontinentia Pigmenti Melanoblastosis Cutis Linearis, Bloch-Siemens-Sulzberger Syndrome, Bloch-Sulzberger Syndrome, Blood types, Blood type A, Blood type B, Blood type AB, Blood type O, Bloom Syndrome, Bloom-Torre-Mackacek Syndrome, Blue Rubber Bleb Nevus, Blue Baby, Blue Diaper Syndrome, BMD, BOD, BOFS, Bone Tumor-Epidermoid Cyst-Polyposis, Bonnet-Dechaume-Blanc Syndrome, Bonnevie-Ulrich Syndrome, Book Syndrome, BOR Syndrome, BORJ, Borjeson Syndrome, Borjeson-Forssman-Lehmann Syndrome, Bowen Syndrome, Bowen-Conradi Syndrome, Bowen-Conradi Hutterite, Bowen-Conradi Type Hutterite Syndrome, Bowman's Layer, BPEI, BPES, Brachial Neuritis, Brachial Neuritis Syndrome, Brachial Plexus Neuritis, Brachial-Plexus-Neuropathy, Brachiocephalic Ischemia, Brachmann-de Lange Syndrome, Brachycephaly, Brachycephaly, Brachymorphic Type Congenital, Bradycardia, Brain Tumors, Brain Tumors Benign, Brain Tumors Malignant, Branched Chain Alpha-Ketoacid Dehydrogenase Deficiency, Branched Chain Ketonuria I, Brancher Deficiency, Branchio-Oculo-Facial Syndrome, Branchio-Oto-Renal Dysplasia, Branchio-Oto-Renal Syndrome,

Branchiooculofacial Syndrome, Branchiootic Syndrome, Brandt Syndrome, Brandywine Type Dentinogenesis Imperfecta, Brandywine type Dentinogenesis Imperfecta, Breast Cancer, BRIC Syndrome, Brittle Bone Disease, Broad Beta Disease, Broad Thumb Syndrome, Broad Thumbs and Great Toes Characteristic Facies and Mental Retardation, Broad Thumb-Hallux, Broca's Aphasia, Brocq-Duhring Disease, Bronze Diabetes, Bronze Schilder's Disease, Brown Albinism, Brown Enamel Hereditary, Brown-Sequard Syndrome, Brown Syndrome, BRRS, Brueghel Syndrome, Bruton's Agammaglobulinemia Common, BS, BSS, Buchanan's Syndrome, Budd's Syndrome, Budd-Chiari Syndrome, Buerger-Gruetz Syndrome, Bulbospinal Muscular Atrophy-X-linked, Bulldog Syndrome, Bullosa Hereditaria, Bullous CIE, Bullous Congenital Ichthyosiform Erythroderma, Bullous Ichthyosis, Bullous Pemphigoid, Burkitt's Lymphoma, Burkitt's Lymphoma African type, Burkitt's Lymphoma Non-african type, BWS, Byler's Disease, C Syndrome, C1 Esterase Inhibitor Dysfunction Type II Angioedema, C1-INH, C1 Esterase Inhibitor Deficiency Type I Angioedema, C1NH, Cacchi-Ricci Disease, CAD, CADASIL, CAH, Calcaneal Valgus, Calcaneovalgus, Calcium Pyrophosphate Dihydrate Deposits, Callosal Agenesis and Ocular Abnormalities, Calves-Hypertrophy of Spinal Muscular Atrophy, Campomelic Dysplasia, Campomelic Dwarfism, Campomelic Syndrome, Camptodactyly-Cleft Palate-Clubfoot, Camptodactyly-Limited Jaw Excursion, Camptomelic Dwarfism, Camptomelic Syndrome, Camptomelic Syndrome Long-Limb Type, Camurati-Engelmann Disease, Canada-Cronkhite Disease, Canavan disease, Canavan's Disease Included, Canavan's Leukodystrophy, Cancer, Cancer Family Syndrome Lynch Type, Cantrell Syndrome, Cantrell-Haller-Ravich Syndrome, Cantrell Pentalogy, Carbamyl Phosphate Synthetase Deficiency, Carbohydrate Deficient Glycoprotein Syndrome, Carbohydrate-Deficient Glycoprotein Syndrome Type Ia, Carbohydrate-Induced Hyperlipemia, Carbohydrate Intolerance of Glucose Galactose, Carbon Dioxide Acidosis, Carboxylase Deficiency Multiple, Cardiac-Limb Syndrome, Cardio-auditory Syndrome, Cardioauditory Syndrome of Jervell and Lange-Nielsen, Cardiocutaneous Syndrome, Cardio-facial-cutaneous syndrome, Cardiofacial Syndrome Cayler Type, Cardiomegalia Glycogenica Diffusa, Cardiomyopathic Lentiginosis, Cardiomyopathy, Cardiomyopathy Associated with Desmin Storage Myopathy, Cardiomyopathy Due to Desmin Defect, Cardiomyopathy-Neutropenia Syndrome, Cardiomyopathy-Neutropenia Syndrome Lethal

Infantile Cardiomyopathy, Cardiopathic Amyloidosis, Cardiospasm, Cardocardiac Syndrome, Carnitine-Acylcarnitine Translocase Deficiency, Carnitine Deficiency and Disorders, Carnitine Deficiency Primary, Carnitine Deficiency Secondary, Carnitine Deficiency Secondary to MCAD Deficiency, Carnitine Deficiency Syndrome, Carnitine Palmitoyl Transferase I & II (CPT I & II), Carnitine Palmitoyltransferase Deficiency, Carnitine Palmitoyltransferase Deficiency Type 1, Carnitine Palmitoyltransferase Deficiency Type 2 benign classical muscular form included severe infantile form included, Carnitine Transport Defect (Primary Carnitine Deficiency), Carnosinase Deficiency, Carnosinemia, Caroli Disease, Carpenter syndrome, Carpenter's, Cartilage-Hair Hypoplasia, Cartilage-Hair Hypoplasia, Castleman's Disease, Castleman's Disease Hyaline Vascular Type, Castleman's Disease Plasma Cell Type, Castleman Tumor, Cat Eye Syndrome, Cat's Cry Syndrome, Catalase deficiency, Cataract-Dental Syndrome, Cataract X-Linked with Hutchinsonian Teeth, Catecholamine hormones, Catel-Manzke Syndrome, Catel-Manzke Type Palatodigital Syndrome, Caudal Dysplasia, Caudal Dysplasia Sequence, Caudal Regression Syndrome, Causalgia Syndrome Major, Cavernomas, Cavernous Angioma, Cavernous Hemangioma, Cavernous Lymphangioma, Cavernous Malformations, Cayler Syndrome, Cazenave's Vitiligo, CBGD, CBPS, CBPS, CCA, CCD, CCHS, CCM Syndrome, CCMS, CCO, CD, CDG1a, CDG1A, CDGS Type Ia, CDGS, CDI, CdLS, Celiac Disease, Celiac sprue, Celiac Sprue-Dermatitis, Cellelar Immunodeficiency with Purine Nucleoside Phosphorylase Deficiency, Celsus' Vitiligo, Central Apnea, Central Core Disease, Central Diabetes Insipidus, Central Form Neurofibromatosis, Central Hypoventilation, Central Sleep Apnea, Centrifugal Lipodystrophy, Centronuclear Myopathy, CEP, Cephalocele, Cephalothoracic Lipodystrophy, Ceramide Trihexosidase Deficiency, Cerebellar Agenesis, Cerebellar Aplasia, Cerebellar Hemiagenesis, Cerebellar Hypoplasia, Cerebellar Vermis Aplasia, Cerebellar Vermis Agenesis-Hypernea-Episodic Eye Moves-Ataxia-Retardation, Cerebellar Syndrome, Cerebellarparenchymal Disorder IV, Cerebellomedullary Malformation Syndrome, Cerebello-Oculocutaneous Telangiectasia, Cerebelloparenchymal Disorder IV Familial, Cerebellopontine Angle Tumor, Cerebral Arachnoiditis, Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukodystrophy, Cerebral Beriberi, Cerebral Diplegia, Cerebral Gigantism, Cerebral

Malformations Vascular, Cerebral Palsy, Cerebro-Oculorenal Dystrophy, Cerebro-Oculo-Facio-Skeletal Syndrome, Cerebrocostomandibular syndrome, Cerebrohepatorenal Syndrome, Cerebromacular Degeneration, Cerebromuscular Dystrophy Fukuyama Type, Cerebroocular Dysgenesis, Cerebroocular Dysplasia-Muscular Dystrophy Syndrome, Cerebrooculofacioskeletal Syndrome, Cerebroretinal Arteriovenous Aneurysm, Cerebroside Lipidosis, Cerebrosidosis, Cerebrotendinous Xanthomatosis, Cerebrovascular Ferrocalcinosis, Ceroid-Lipofuscinosis Adult form, Cervical Dystonia, Cervico-Oculo-Acoustic Syndrome, Cervical Spinal Stenosis, Cervical Vertebral Fusion, CES, CF, CFC syndrome, CFIDS, CFND, CGD, CGF, CGF, Chalasodermia Generalized, Chanarin Dorfman Disease, Chanarin Dorfman Syndrome, Chanarin Dorfman Ichthyosis Syndrome, Chandler's Syndrome, Charcot's Disease, Charcot-Marie-Tooth, Charcot-Marie-Tooth Disease, Charcot-Marie-Tooth Disease Variant, Charcot-Marie-Tooth-Roussy-Levy Disease, CHARGE Association, Charge Syndrome, CHARGE Syndrome, Chaund's Ectodermal Dysplasias, Chediak-Higashi Syndrome, Chediak-Steinbrinck-Higashi Syndrome, Cheilitis Granulomatosa, Cheiloschisis, Chemke Syndrome, Cheney Syndrome, Cherry Red Spot and Myoclonus Syndrome, CHF, CHH, Chiari's Disease, Chiari Malformation I, Chiari Malformation, Chiari Type I (Chiari Malformation I), Chiari Type II (Chiari Malformation II), Chiari I Syndrome, Chiari-Budd Syndrome, Chiari-Frommel Syndrome, Chiari Malformation II, CHILD Syndrome, CHILD Ichthyosis Syndrome, CHILD Syndrome Ichthyosis, Childhood Adrenoleukodystrophy, Childhood Dermatomyositis, Childhood-onset Dystonia, Childhood Cyclic Vomiting, Childhood Giant Axonal Neuropathy, Childhood Hypophasphatasia, Childhood Muscular Dystrophy, CHN, Cholestasis, Cholestasis Hereditary Norwegian Type, Cholestasis Intrahepatic, Cholestasis Neonatal, Cholestasis of Oral Contraceptive Users, Cholestasis with Peripheral Pulmonary Stenosis, Cholestasis of Pregnancy, Cholesterol Desmolase Deficiency, Chondrodysplasia Punctata, Chondrodystrophia Calcificans Congenita, Chondrodystrophia Fetalis, Chondrodystrophic Myotonia, Chondrodystrophy, Chondrodystrophy with Clubfeet, Chondrodystrophy Epiphyseal, Chondrodystrophy Hyperplastic Form, Chondroectodermal Dysplasias, Chondrogenesis Imperfecta, Chondrohystrophia, Chondroosteodystrophy, Choreoacanthocytosis, Chorionic Villi Sampling, Chorioretinal Anomalies, Chorioretinal Anomalies with ACC, Chorireninal Coloboma-Joubert

Syndrome, Choroidal Sclerosis, Choroideremia, Chotzen Syndrome, Chotzen Syndrome, Christ-Siemens-Touraine Syndrome, Christ-Siemans-Touraine Syndrome, Christmas Disease, Christmas Tree Syndrome, Chromosome 3 Deletion of Distal 3p, Chromosome 3 Distal 3p Monosomy, Chromosome 3-Distal 3q2 Duplication, Chromosome 3-Distal 3q2 Trisomy, Chromosome 3 Monosomy 3p2, Chromosome 3q Partial Duplication Syndrome, Chromosome 3q, Partial Trisomy Syndrome, Chromosome 3-Trisomy 3q2, Chromosome 4 Deletion 4q31-qter Syndrome, Chromosome 4 Deletion 4q32-qter Syndrome, Chromosome 4 Deletion 4q33-qter Syndrome, Chromosome 4 Long Arm Deletion, Chromosome 4 Monosomy 4q, Chromosome 4-Monosomy 4q, Chromosome 4 Monosomy Distal 4q, Chromosome 4 Partial Deletion 4p, Chromosome 4 Partial Deletion of the Short Arm, Chromosome 4 Partial Monosomy of Distal 4q, Chromosome 4 Partial Monosomy 4p, Chromosome 4 Partial Trisomy 4 (q25-qter), Chromosome 4 Partial Trisomy 4 (q26 or q27-qter), Chromosome 4 Partial Trisomy 4 (q31 or 32-qter), Chromosome 4 Partial Trisomy 4p, Chromosome 4 Partial Trisomies 4q2 and 4q3, Chromosome 4 Partial Trisomy Distal 4, Chromosome 4 Ring, Chromosome 4 4q Terminal Deletion Syndrome, Chromosome 4q- Syndrome, Chromosome 4 Trisomy 4, Chromosome 4 Trisomy 4p, Chromosome 4 XY/47 XXY (Mosaic), Chromosome 5 Monosomy 5p, Chromosome 5, Partial Deletion of the Short Arm Syndrome, Chromosome 5 Trisomy 5p, Chromosome 5 Trisomy 5p Complete (5p11-pter), Chromosome 5 Trisomy 5p Partial (5p13 or 14-pter), Chromosome 5p-Syndrome, Chromosome 6 Partial Trisomy 6q, Chromosome 6 Ring, Chromosome 6 Trisomy 6q2, Chromosome 7 Monosomy 7p2, Chromosome 7 Partial Deletion of Short Arm (7p2-), Chromosome 7 Terminal 7p Deletion [del (7) (p21-p22)], Chromosome 8 Monosomy 8p2, Chromosome 8 Monosomy 8p21-pter, Chromosome 8 Partial Deletion (short arm), Chromosome 8 Partial Monosomy 8p2, Chromosome 9 Complete Trisomy 9P, Chromosome 9 Partial Deletion of Short Arm, Chromosome 9 Partial Monosomy 9p, Chromosome 9 Partial Monosomy 9p22, Chromosome 9 Partial Monosomy 9p22-pter, Chromosome 9 Partial Trisomy 9P Included, Chromosome 9 Ring, Chromosome 9 Tetrasomy 9p, Chromosome 9 Tetrasomy 9p Mosaicism, Chromosome 9 Trisomy 9p (Multiple Variants), Chromosome 9 Trisomy 9 (pter-p21 to q32) Included, Chromosome 9 Trisomy Mosaic, Chromosome 10 Distal Trisomy 10q, Chromosome 10 Monosomy, Chromosome 10 Monosomy 10p, Chromosome 10, Partial Deletion (short

arm), Chromosome 10, 10p- Partial, Chromosome 10 Partial Trisomy 10q24-qter, Chromosome 10 Trisomy 10q2, Partial Monosomy of Long Arm of Chromosome 11, Chromosome 11 Partial Monosomy 11q, Chromosome 11 Partial Trisomy, Chromosome 11 Partial Trisomy 11q13-qter, Chromosome 11 Partial Trisomy 11q21-qter, Chromosome 11 Partial Trisomy 11q23-qter, Chromosome 11q,Partial Trisomy, Chromosome 12 Isochromosome 12p Mosaic, Chromosome 13 Partial Monosomy 13q, Chromosome 13, Partial Monosomy of the Long Arm, Chromosome 14 Ring, Chromosome 14 Trisomy, Chromosome 15 Distal Trisomy 15q, Chromosome r15, Chromosome 15 Ring, Chromosome 15 Trisomy 15q2, Chromosome 15q, Partial Duplication Syndrome, Chromosome 17 Interstitial Deletion 17p, Chromosome 18 Long Arm Deletion Syndrome, Chromosome 18 Monosomy 18p, Chromosome 18 Monosomy 18Q, Chromosome 18 Ring, Chromosome 18 Tetrasomy 18p, Chromosome 18q- Syndrome, Chromosome 21 Mosaic 21 Syndrome, Chromosome 21 Ring, Chromosome 21 Translocation 21 Syndrome, Chromosome 22 Inverted Duplication (22pter-22q11), Chromosome 22 Partial Trisomy (22pter-22q11), Chromosome 22 Ring, Chromosome 22 Trisomy Mosaic, Chromosome 48 XXYY, Chromosome 48 XXXY, Chromosome r15, Chromosomal Triplication, Chromosome Triploidy Syndrome, Chromosome X, Chromosome XXY, Chronic Acholuric Jaundice, Chronic Adhesive Arachnoiditis, Chronic Adrenocortical Insufficiency, Chronic Cavernositis, Chronic Congenital Aregenerative Anemia, Chronic Dysphagocytosis, Chronic Familial Granulomatosis, Chronic Familial Icterus, Chronic Fatigue Immune Dysfunction Syndrome (CFIDS), Chronic Granulomatous Disease, Chronic Guillain-Barre Syndrome, Chronic Idiopathic Jaundice, Chronic Idiopathic Polyneuritis (CIP), Chronic Inflammatory Demyelinating Polyneuropathy, Chronic Inflammatory Demyelinating Polyradiculoneuropathy, Chronic Motor Tic, Chronic Mucocutaneous Candidiasis, Chronic Multiple Tics, Chronic Non-Specific Ulcerative Colitis, Chronic Obliterative Cholangitis, Chronic Peptic Ulcer and Esophagitis Syndrome, Chronic Progressive Chorea, Chronic Progressive External Ophthalmoplegia Syndrome, Chronic Progressive External Ophthalmoplegia and Myopathy, Chronic Progressive External Ophthalmoplegia with Ragged Red Fibers, Chronic Relapsing Polyneuropathy, Chronic Sarcoidosis, Chronic Spasmodic Dysphonia, Chronic Vomiting in Childhood, CHS, Churg-Strauss Syndrome, Cicatricial Pemphigoid, CIP, Cirrhosis Congenital

Pigmentary, Cirrhosis, Cistinuria, Citrullinemia, CJD, Classic Schindler Disease, Classic Type Pfeiffer Syndrome, Classical Maple Syrup Urine Disease, Classical Hemophilia, Classical Form Cockayne Syndrome Type I (Type A), Classical Leigh's Disease, Classical Phenylketonuria, Classical X-Linked Pelizaeus-Merzbacher Brain Sclerosis, CLE, Cleft Lip/Palate Mucous Cysts Lower Lip PP Digital and Genital Anomalies, Cleft Lip-Palate Blepharophimosis Lagophthalmos and Hypertelorism, Cleft Lip/Palate with Abnormal Thumbs and Microcephaly, Cleft palate-joint contractures-dandy walker malformations, Cleft Palate and Cleft Lip, Cleidocranial Dysplasia w/ Micrognathia, Absent Thumbs, & Distal Aphalangia, Cleidocranial Dysostosis, Cleidocranial Dysplasia, Click murmur syndrome, CLN1, Clonic Spasmodic, Cloustons Syndrome, Clubfoot, CMDI, CMM, CMT, CMTC, CMTX, COA Syndrome, Coarctation of the aorta, Coats' Disease, Cobblestone dysplasia, Cochin Jewish Disorder, Cockayne Syndrome, COD-MD Syndrome, COD, Coffin Lowry Syndrome, Coffin Syndrome, Coffin Siris Syndrome, COFS Syndrome, Cogan Corneal Dystrophy, Cogan Reese Syndrome, Cohen Syndrome, Cold Agglutinin Disease, Cold Antibody Disease, Cold Antibody Hemolytic Anemia, Cold Agglutinin Disease, Colitis Ulcerative, Colitis Gravis, Colitis Gravis, Colitis Ulcerative Chronic Non-Specific Ulcerative Colitis, Collodion Baby, Coloboma Heart Defects Atresia of the Choanae Retardation of Growth and Development Genital and Urinary Anomalies and Ear Anomalies, Coloboma, Colonic Neurosis, Colour blindness, Colpocephaly, Columnar-Like Esophagus, Combined Cone-Rod Degeneration, Combined Immunodeficiency with Immunoglobulins, Combined Mesoectodermal Dysplasia, Common Variable Hypogammaglobulinemia, Common Variable Immunodeficiency, Common Ventricle, Communicating Hydrocephalus, Complete Absense of Hypoxanthine-Guanine Phosphoribosyltranferase, Complete Atrioventricular Septal Defect, Complement Component 1 Inhibitor Deficiciency, Complement Component C1 Regulatory Component Deficiency, Complete Heart Block, Complex Carbohydrate Intolerance, Complex Regional Pain Syndrome, Complex V ATP Synthase Deficiency, Complex I, Complex I NADH dehydrogenase deficiency, Complex II, Complex II Succinate dehydrogenase deficiency, Complex III, Complex III Ubiquinone-cytochrome c oxidoreductase deficiency, Complex IV, Complex IV Cytochrome c oxidase deficiency, Complex IV Deficiency, Complex V, Cone-Rod Degeneration, Cone-Rod Degeneration Progressive, Cone Dystrophy, Cone-

Rod Dystrophy, Confluent Reticular Papillomatosis, Congenital with low PK Kinetics, Congenital Absence of Abdominal Muscles, Congenital Absence of the Thymus and Parathyroids, Congenital Achromia, Congenital Addison's Disease, Congenital Adrenal Hyperplasia, Congenital Adreneal Hyperplasia, Congenital Afibrinogenemia, Congenital Alveolar Hypoventilation, Congenital Anemia of Newborn, Congenital Bilateral Persylvian Syndrome, Congenital Brown Syndrome, Congenital Cardiovascular Defects, Congenital Central Hypoventilation Syndrome, Congenital Cerebral Palsy, Congenital Cervical Synostosis, Congenital Clasped Thumb with Mental Retardation, Congenital Contractural Arachnodactyly, Congenital Contractures Multiple with Arachnodactyly, Congenital Cyanosis, Congenital Defect of the Skull and Scalp, Congenital Dilatation of Intrahepatic Bile Duct, Congenital Dysmyelinating Neuropathy, Congenital Dysphagocytosis, Congenital Dysplastic Angiectasia, Congenital Erythropoietic Porphyria, Congenital Erythropoietic Porphyria, Congenital Factor XIII Deficiency, Congenital Failure of Autonomic Control of Respiration, Congenital Familial Nonhemolytic Jaundice Type I, Congenital Familial Protracted Diarrhea, Congenital Form Cockayne Syndrome Type II (Type B), Congenital Generalized Fibromatosis, Congenital German Measles, Congenital Giant Axonal Neuropathy, Congenital Heart Block, Congenital Heart Defects, Congenital Hemidysplasia with Ichthyosis Erythroderma and Limb Defects, Congenital Hemolytic Jaundice, Congenital Hemolytic Anemia, Congenital Hepatic Fibrosis, Congenital Hereditary Corneal Dystrophy, Congenital Hereditary Lymphedema, Congenital Hyperchondroplasia, Congenital Hypomyelinating Polyneuropathy, Congenital Hypomyelination Neuropathy, Congenital Hypomyelination, Congenital Hypomyelination (Onion Bulb) Polyneuropathy, Congenital Ichthyosiform Erythroderma, Congenital Keratoconus, Congenital Lactic Acidosis, Congenital Lactose Intolerance, Congenital Lipodystrophy, Congenital Liver Cirrhosis, Congenital Lobar Emphysema, Congenital Localized Emphysema, Congenital Macroglossia, Congenital Medullary Stenosis, Congenital Megacolon, Congenital Melanocytic Nevus, Congenital Mesodermal Dysmorphodystrophy, Congenital Mesodermal Dystrophy, Congenital Microvillus Atrophy, Congenital Multiple Arthrogryposis, Congenital Myotonic Dystrophy, Congenital Neuropathy caused by Hypomyelination, Congenital Pancytopenia, Congenital Pernicious Anemia, Congenital Pernicious Anemia due to Defect of Intrinsic Factor,

Congenital Pernicious Anemia due to Defect of Intrinsic Factor, Congenital Pigmentary Cirrhosis, Congenital Porphyria, Congenital Proximal Myopathy Associated with Desmin Storage Myopathy, Congenital Pulmonary Emphysema, Congenital Pure Red Cell Anemia, Congenital Pure Red Cell Aplasia, Congenital Retinal Blindness, Congenital Retinal Cyst, Congenital Retinitis Pigmentosa, Congenital Retinoschisis, Congenital Rod Disease, Congenital Rubella Syndrome, Congenital Scalp Defects with Distal Limb Reduction Anomalies, Congenital Sensory Neuropathy, Congenital SMA with arthrogryposis, Congenital Spherocytic Anemia, Congenital Spondyloepiphyseal Dysplasia, Congenital Tethered Cervical Spinal Cord Syndrome, Congenital Tyrosinosis, Congenital Varicella Syndrome, Congenital Vascular Cavernous Malformations, Congenital Vascular Veils in the Retina, Congenital Word Blindness, Congenital Wandering Spleen (Pediatric), Congestive Cardiomyopathy, Conical Cornea, Conjugated Hyperbilirubinemia, Conjunctivitis, Conjunctivitis Ligneous, Conjunctivo-Urethro-Synovial Syndrome, Conn's Syndrome, Connective Tissue Disease, Conradi Disease, Conradi Hunermann Syndrome, Constitutional Aplastic Anemia, Constitutional Erythroid Hypoplasia, Constitutional Eczema, Constitutional Liver Dysfunction, Constitutional Thrombopathy, Constricting Bands Congenital, Constrictive Pericarditis with Dwarfism, Continuous Muscle Fiber Activity Syndrome, Contractural Arachnodactyly, Contractures of Feet Muscle Atrophy and Oculomotor Apraxia, Convulsions, Cooley's anemia, Copper Transport Disease, Coproporphyria Porphyria Hepatica, Cor Triatriatum, Cor Triatriatum Sinistrum, Cor Triloculare Biatriatum, Cor Biloculare, Cori Disease, Cornea Dystrophy, Corneal Amyloidosis, Corneal Clouding-Cutis Laxa-Mental Retardation, Corneal Dystrophy, Cornelia de Lange Syndrome, Coronal Dentine Dysplasia, Coronary Artery Disease, Coronary Heart Disease, Corpus Callosum Agenesis, Cortical-Basal Ganglionic Degeneration, Corticalis Deformaris, Cortico-Basal Ganglionic Degeneration (CBGD), Corticobasal Degeneration, Corticosterone Methloxidase Deficiency Type I, Corticosterone Methyloxidase Deficiency Type II, Cortisol, Costello Syndrome, Cot Death, COVESDEM Syndrome, COX, COX Deficiency, COX Deficiency French-Canadian Type, COX Deficiency Infantile Mitochondrial Myopathy de Toni-Fanconi-Debre included, COX Deficiency Type Benign Infantile Mitochondrial Mypoathy, CP, CPEO, CPEO with Myopathy, CPEO with Ragged-Red Fibers, CPPD Familial Form, CPT

Deficiency, CPTD, Cranial Arteritis, Cranial Meningoencephalocele, Cranio-Oro-Digital Syndrome, Craniocarpotarsal dystrophy, Craniocele, Craniodigital Syndrome-Mental Retardation Scott Type, Craniofacial Dysostosis, Craniofacial Dysostosis-PD Arteriosus-Hypertrichosis-Hypoplasia of Labia, Craniofrontonasal Dysplasia, Craniometaphyseal Dysplasia, Cranioorodigital Syndrome, Cranioorodigital Syndrome Type II, Craniostenosis Crouzon Type, Craniostenosis, Craniosynostosis-Choanal Atresia-Radial Humeral Synostosis, Craniosynostosis-Hypertrichosis-Facial and Other Anomalies, Craniosynostosis Midfacial Hypoplasia and Foot Abnormalities, Craniosynostosis Primary, Craniosynostosis-Radial Aplasia Syndrome, Craniosynostosis with Radial Defects, Cranium Bifidum, CREST Syndrome, Creutzfeldt Jakob Disease, Cri du Chat Syndrome, Crib Death, Crigler Najjar Syndrome Type I, Crohn's Diseas, Cronkhite-Canada Syndrome, Cross Syndrome, Cross' Syndrome, Cross-McKusick-Breen Syndrome, Crouzon, Crouzon Syndrome, Crouzon Craniofacial Dysostosis, Cryoglobulinemia Essential Mixed, Cryptophthalmos-Syndactyly Syndrome, Cryptorchidism-Dwarfism-Subnormal Mentality, Crystalline Corneal Dystrophy of Schnyder, CS, CSD, CSID, CSO, CST Syndrome, Curly Hair-Ankyloblephanon-Nail Dysplasia, Curschmann-Batten-Steinert Syndrome, Curth Macklin Type Ichthyosis Hystric, Curth-Macklin Type, Cushing's, Cushing Syndrome, Cushing's III, Cutaneous Malignant Melanoma Hereditary, Cutaneous Porphyrias, Cutis Laxa, Cutis Laxa-Growth Deficiency Syndrome, Cutis Marmorata Telangiectatica Congenita, CVI, CVID, CVS, Cyclic vomiting syndrome, Cystic Disease of the Renal Medulla, Cystic Hygroma, Cystic Fibrosis, Cystic Lymphangioma, Cystine-Lysine-Arginine-Ornithinuria, Cystine Storage Disease, Cystinosis, Cystinuria, Cystinuria with Dibasic Aminoaciduria, Cystinuria Type I, Cystinuria Type II, Cystinuria Type III, Cysts of the Renal Medulla Congenital, Cytochrome C Oxidase Deficiency, D.C., Dacryosialoadenopathy, Dacryosialoadenopathia, Dalpro, Dalton, Daltonism, Danbolt-Cross Syndrome, Dancing Eyes-Dancing Feet Syndrome, Dandy-Walker Syndrome, Dandy-Walker Cyst, Dandy-Walker Deformity, Dandy Walker Malformation, Danish Cardiac Type Amyloidosis (Type III), Darier Disease, Davidson's Disease, Davies' Disease, DBA, DBS, DC, DD, De Barsy Syndrome, De Barsy-Moens-Diercks Syndrome, de Lange Syndrome, De Morsier Syndrome, De. Santis Cacchione Syndrome, de Toni-Fanconi Syndrome, Deafness

Congenital and Functional Heart Disease, Deafness-Dwarfism-Retinal Atrophy, Deafness-Functional Heart Disease, Deafness Onychodystrophy Osteodystrophyand Mental Retardation, Deafness and Pili Torti Bjornstad Type, Deafness Sensorineural with Imperforate Anus and Hypoplastic Thumbs, Debrancher Deficiency, Deciduous Skin, Defect of Enterocyte Intrinsic Factor Receptor, Defect in Natural Killer Lymphocytes, Defect of Renal Reabsorption of Carnitine, Deficiency of Glycoprotein Neuraminidase, Deficiency of Mitochondrial Respiratory Chain Complex IV, Deficiency of Platelet Glycoprotein Ib, Deficiency of Von Willebrand Factor Receptor, Deficiency of Short-Chain Acyl-CoA Dehydrogenase (ACADS, Deformity with Mesomelic Dwarfism, Degenerative Chorea, Degenerative Lumbar Spinal Stenosis, Degos Disease, Degos-Kohlmeier Disease, Degos Syndrome, DEH, Dejerine-Roussy Syndrome, Dejerine Sottas Disease, Deletion 9p Syndrome Partial, Deletion 11q Syndrome Partial, Deletion 13q Syndrome Partial, Delleman-Oorthuys Syndrome, Delleman Syndrome, Dementia with Lobar Atrophy and Neuronal Cytoplasmic Inclusions, Demyelinating Disease, DeMyer Syndrome, Dentin Dysplasia Coronal, Dentin Dysplasia Radicular, Dentin Dysplasia Type I, Dentin Dysplasia Type II, Dentinogenesis Imperfecta Brandywine type, Dentinogenesis Imperfecta Shields Type, Dentinogenesis Imperfecta Type III, Dento-Oculo-Osseous Dysplasia, Dentooculocutaneous Syndrome, Denys-Drash Syndrome, Depakene, DepakeneTM exposure, Depakote, Depakote Sprinkle, Depigmentation-Gingival Fibromatosis-Microphthalmia, Dercum Disease, Dermatitis Atopic, Dermatitis Exfoliativa, Dermatitis Herpetiformis, Dermatitis Multiformis, Dermatochalasia Generalized, Dermatolysis Generalized, Dermatomegaly, Dermatomyositis sine myositis, Dermatomyositis, Dermatosparaxis, Dermatostomatitis Stevens Johnson Type, Desbuquois Syndrome, Desmin Storage Myopathy, Desquamation of Newborn, Deuteranomaly, Developmental Reading Disorder, Developmental Gerstmann Syndrome, Devergie Disease, Devic Disease, Devic Syndrome, Dextrocardia- Bronchiectasis and Sinusitis, Dextrocardia with Situs Inversus, DGS, DGSX Golabi-Rosen Syndrome Included, DH, DHAP alkyl transferase deficiency, DHBS Deficiency, DHBS Deficiency, DHOF, DHPR Deficiency, Diabetes Insipidus, Diabetes Insipidus Diabetes Mellitus Optic Atrophy and Deafness, Diabetes Insipidus Neurohypophyseal, Diabetes Insulin Dependent, Diabetes Mellitus, Diabetes Mellitus Addison's Disease Myxedema, Diabetic Acidosis, Diabetic

Bearded Woman Syndrome, Diamond-Blackfan Anemia, Diaphragmatic Apnea, Diaphyseal Aclasis, Diastrophic Dwarfism, Diastrophic Dysplasia, Diastrophic Nanism Syndrome, Dicarboxylic Aminoaciduria, Dicarboxylicaciduria Caused by Defect in Beta-Oxidation of Fatty Acids, Dicarboxylicaciduria due to Defect in Beta-Oxidation of Fatty Acids, Dicarboxylicaciduria due to MCADH Deficiency, Dichromasy, Dicker-Opitz, DIDMOAD, Diencephalic Syndrome, Diencephalic Syndrome of Childhood, Diencephalic Syndrome of Emaciation, Dienoyl-CoA Reductase Deficiency, Diffuse Cerebral Degeneration in Infancy, Diffuse Degenerative Cerebral Disease, Diffuse Idiopathic Skeletal Hyperostosis, Diffusum-Glycopeptiduria, DiGeorge Syndrome, Digital-Oro-Cranio Syndrome, Digito-Oto-Palatal Syndrome, Digito-Oto-Palatal Syndrome Type I, Digito-Oto-Palatal Syndrome Type II, Dihydrobiopterin Synthetase Deficiency, Dihydropteridine Reductase Deficiency, Dihydroxyacetonephosphate synthase, Dilated (Congestive) Cardiomyopathy, Dimitri Disease, Diplegia of Cerebral Palsy, Diplo-Y Syndrome, Disaccharidase Deficiency, Disaccharide Intolerance I, Discoid Lupus, Discoid Lupus Erythematosus, DISH, Disorder of Cornification, Disorder of Cornification Type I, Disorder of Cornification 4, Disorder of Cornification 6, Disorder of Cornification 8, Disorder of Cornification 9 Netherton's Type, Disorder of Cornification 11 Phytanic Acid Type, Disorder of Cornification 12 (Neutral Lipid Storage Type), Disorder of Conification 13, Disorder of Cornification 14, Disorder of Cornification 14 Trichothiodystrophy Type, Disorder of Cornification 15 (Keratitis Deafness Type), Disorder of Cornification 16, Disorder of Cornification 18 Erythrokeratodermia Variabilis Type, Disorder of Cornification 19, Disorder of Cornification 20, Disorder of Cornification 24, Displaced Spleen, Disseminated Lupus Erythematosus, Disseminated Neurodermatitis, Disseminated Sclerosis, Distal 11q Monosomy, Distal 11q- Syndrome, Distal Arthrogryposis Multiplex Congenita Type IIA, Distal Arthrogryposis Multiplex Congenita Type IIA, Distal Arthrogryposis Type IIA, Distal Arthrogryposis Type 2A, Distal Duplication 6q, Distal Duplication 10q, Dup(10q) Syndrome, Distal Duplication 15q, Distal Monosomy 9p, Distal Trisomy 6q, Distal Trisomy 10q Syndrome, Distal Trisomy 11q, Divalproex, DJS, DKC, DLE, DLPIII, DM, DMC Syndrome, DMC Disease, DMD, DNS Hereditary, DOC I, DOC 2, DOC 4, DOC 6 (Harlequin Type), DOC 8 Curth-Macklin Type, DOC 11 Phytanic Acid Type, DOC 12 (Neutral Lipid Storage Type), DOC 13, DOC 14, DOC 14

Trichothiodystrophy Type, DOC 15 (Keratitis Deafness Type), DOC 16, DOC 16 Unilateral Hemidysplasia Type, DOC 18, DOC 19, DOC 20, DOC 24, Dohle's Bodies-Myelopathy, Dolichospondylic Dysplasia, Dolichostenomelia, Dolichostenomelia Syndrome, Dominant Type Kenny-Caffe Syndrome, Dominant Type Myotonia Congenita, Donahue Syndrome, Donath-Landsteiner Hemolytic Anemia, Donath-Landsteiner Syndrome, DOOR Syndrome, DOORS Syndrome, Dopa-responsive Dystonia (DRD), Dorfman Chanarin Syndrome, Dowling-Meara Syndrome, Down Syndrome, DR Syndrome, Drash Syndrome, DRD, Dreifuss-Emery Type Muscular Dystrophy with Contractures, Dressler Syndrome, Drifting Spleen, Drug-induced Acanthosis Nigricans, Drug-induced Lupus Erythematosus, Drug-related Adrenal Insufficiency, Drummond's Syndrome, Dry Beriberi, Dry Eye, DTD, Duane's Retraction Syndrome, Duane Syndrome, Duane Syndrome Type IA 1B and 1C, Duane Syndrome Type 2A 2B and 2C, Duane Syndrome Type 3A 3B and 3C, Dubin Johnson Syndrome, Dubowitz Syndrome, Duchenne, Duchenne Muscular Dystrophy, Duchenne's Paralysis, Duhring's Disease, Duncan Disease, Duncan's Disease, Duodenal Atresia, Duodenal Stenosis, Duodenitis, Duplication 4p Syndrome, Duplication 6q Partial, Dupuy's Syndrome, Dupuytren's Contracture, Dutch-Kennedy Syndrome, Dwarfism, Dwarfism Campomelic, Dwarfism Cortical Thickening of the Tubular Bones & Transient Hypocalcemia, Dwarfism Levi's Type, Dwarfism Metatropic, Dwarfism-Onychodysplasia, Dwarfism-Pericarditis, Dwarfism with Renal Atrophy and Deafness, Dwarfism with Rickets, DWM, Dyggve Melchior Clausen Syndrome, Dysautonomia Familial, Dysbetalipoproteinemia Familial, Dyschondrodysplasia with Hemangiomas, Dyschondrosteosis, Dyschromatosis Universalis Hereditaria, Dysencephalia Splanchnocystica, Dyskeratosis Congenita, Dyskeratosis Congenita Autosomal Recessive, Dyskeratosis Congenita Scoggins Type, Dyskeratosis Congenita Syndrome, Dyskeratosis Follicularis Vegetans, Dyslexia, Dysmyelogenic Leukodystrophy, Dysmyelogenic Leukodystrophy-Megalobare, Dysphonia Spastica, Dysplasia Epiphysialis Punctata, Dysplasia Epiphyseal Hemimelica, Dysplasia of Nails With Hypodontia, Dysplasia Cleidocranial, Dysplasia Fibrous, Dysplasia Gigantism SyndromeX-Linked, Dysplasia Osteodental, Dysplastic Nevus Syndrome, Dysplastic Nevus Type, Dyssynergia Cerebellaris Myoclonica, Dyssynergia Esophagus, Dystonia, Dystopia Canthorum, Dystrophia Adiposogenitalis, Dystrophia Endothelialis Cornea,

Dystrophia Mesodermalis, Dystrophic Epidermolysis Bullosa, Dystrophy, Asphyxiating Thoracic, Dystrophy Myotonic, E-D Syndrome, Eagle-Barrett Syndrome, Eales Retinopathy, Eales Disease, Ear Anomalies-Contractures-Dysplasia of Bone with Kyphoscoliosis, Ear Patella Short Stature Syndrome, Early Constraint Defects, Early Hypercalcemia Syndrome with Elfin Facie, Early-onset Dystonia, Eaton Lambert Syndrome, EB, Ebstein's anomaly, EBV Susceptibility (EBVS), EBVS, ECD, ECPSG, Ectodermal Dysplasias, Ectodermal Dysplasia Anhidrotic with Cleft Lip and Cleft Palate, Ectodermal Dysplasia-Exocrine Pancreatic Insufficiency, Ectodermal Dysplasia Rapp-Hodgkin type, Ectodermal and Mesodermal Dysplasia Congenital, Ectodermal and Mesodermal Dysplasia with Osseous Involvement, Ectodermosis Erosiva Pluriorificialis, Ectopia Lentis, Ectopia Vesicae, Ectopic ACTH Syndrome, Ectopic Adrenocorticotropic Hormone Syndrome, Ectopic Anus, Ectrodactilia of the Hand, Ectrodactyly, Ectrodactyly-Ectodermal Dysplasia-Clefting Syndrome, Ectrodactyly Ectodermal Dysplasias Clefting Syndrome, Ectrodactyly Ectodermal Dysplasia Cleft Lip/Cleft Palate, Eczema, Eczema-Thrombocytopenia-Immunodeficiency Syndrome, EDA, EDMD, EDS, EDS Arterial-Ecchymotic Type, EDS Arthrochalasia, EDS Classic Severe Form, EDS Dysfibronectinemic, EDS Gravis Type, EDS Hypermobility, EDS Kyphoscoliotic, EDS Kyphoscoliosis, EDS Mitis Type, EDS Ocular-Scoliotic, EDS Progeroid, EDS Periodontosis, EDS Vascular, EEC Syndrome, EFE, EHBA, EHK, Ehlers Danlos Syndrome, Ehlers-Danlos syndrome, Ehlers Danlos IX, Eisenmenger Complex, Eisenmenger's complex, Eisenmenger Disease, Eisenmenger Reaction, Eisenmenger Syndrome, Ekbom Syndrome, Ekman-Lobstein Disease, Ektrodactyly of the Hand, EKV, Elastin fiber disorders, Elastorrhexis Generalized, Elastosis Dystrophica Syndrome, Elective Mutism (obsolete), Elective Mutism, Electrocardiogram (ECG or EKG), Electron Transfer Flavoprotein (ETF) Dehydrogenase Deficiency: (GAII & MADD), Electrophysiologic study (EPS), Elephant Nails From Birth, Elephantiasis Congenita Angiomatosa,Hemangiectatic Hypertrophy, Elfin Facies with Hypercalcemia, Ellis-van Creveld Syndrome, Ellis Van Creveld Syndrome, Embryoma Kidney, Embryonal Adenomyosarcoma Kidney, Embryonal Carcinosarcoma Kidney, Embryonal Mixed Tumor Kidney, EMC, Emery Dreyfus Muscular Dystrophy, Emery-Dreifuss Muscular Dystrophy, Emery-Dreifuss Syndrome, EMF, EMG Syndrome, Empty Sella Syndrome,

Encephalitis Periaxialis Diffusa, Encephalitis Periaxialis Concentrica, Encephalocele, Encephalofacial Angiomatosis, Encephalopathy, Encephalotrigeminal Angiomatosis, Enchondromatosis with Multiple Cavernous Hemangiomas, Endemic Polyneuritis, Endocardial Cushion Defect, Endocardial Cushion Defects, Endocardial Dysplasia, Endocardial Fibroelastosis (EFE), Endogenous Hypertriglyceridemia, Endolymphatic Hydrops, Endometrial Growths, Endometriosis, Endomyocardial Fibrosis, Endothelial Corneal Dystrophy Congenital, Endothelial Epithelial Corneal Dystrophy, Endothelium, Engelmann Disease, Enlarged Tongue, Enterocolitis, Enterocyte Cobalamin Malabsorption, Eosinophia Syndrome, Eosinophilic Cellulitis, Eosinophilic Fasciitis, Eosinophilic Granuloma, Eosinophilic Syndrome, Epidermal Nevus Syndrome, Epidermolysis bullosa, Epidermolysis Bullosa, Epidermolysis Bullosa Acquisita, Epidermolysis Bullosa Hereditaria, Epidermolysis Bullosa Letalias, Epidermolysis Hereditaria Tarda, Epidermolytic Hyperkeratosis, Epidermolytic Hyperkeratosis (Bullous CIE), Epilepsia Procursiva, Epilepsy, Epinephrine, Epiphyseal Changes and High Myopia, Epiphyseal Osteochondroma Benign, Epiphysealis Hemimelica Dysplasia, Episodic-Abnormal Eye Movement, Epithelial Basement Membrane Corneal Dystrophy, Epithelial Corneal Dystrophy of Meesmann Juvenile, Epitheliomatosis Multiplex with Nevus, Epithelium, Epival, EPS, Epstein-Barr Virus-Induced Lymphoproliferative Disease in Males, Erb-Goldflam syndrome, Erdheim Chester Disease, Erythema Multiforme Exudativum, Erythema Polymorphe Stevens Johnson Type, Erythroblastophthisis, Erythroblastosis Fetalis, Erythroblastosis Neonatorum, Erythroblastotic Anemia of Childhood, Erythrocyte Phosphoglycerate Kinase Deficiency, Erythrogenesis Imperfecta, Erythrokeratodermia Progressiva Symmetrica, Erythrokeratodermia Progressiva Symmetrica Ichthyosis, Erythrokeratodermia Variabilis, Erythrokeratodermia Variabilis, Erythrokeratodermia Variabilis Type, Erythrokeratolysis Hiemalis, Erythrokeratolysis Hiemalis, Erythrokeratolysis Hiemalis, Erythropoietic Porphyrias, Erythropoietic Porphyria, Escobar Syndrome, Esophageal Atresia, Esophageal Aperistalsis, Esophagitis-Peptic Ulcer, Esophagus Atresia and/or Tracheoesophageal Fistula, Essential Familial Hyperlipemia, Essential Fructosuria, Essential Hematuria, Essential Hemorrhagic Thrombocythemia, Essential Mixed Cryoglobulinemia, Essential Moschowitz Disease, Essential Thrombocythemia, Essential Thrombocytopenia, Essential Thrombocytosis,

Essential Tremor, Esterase Inhibitor Deficiency, Estren-Dameshek variant of Fanconi Anemia, Estrogen-related Cholestasis, ET, ETF, Ethylmalonic Adipicaciduria, Eulenburg Disease, pc, EVCS, Exaggerated Startle Reaction, Exencephaly, Exogenous Hypertriglyceridemia, Exomphalos-Macroglossia-Gigantism Syndrome, Exophthalmic Goiter, Expanded Rubella Syndrome, Exstrophy of the Bladder, EXT, External Chondromatosis Syndrome, Extrahepatic Biliary Atresia, Extramedullary Plasmacytoma, Exudative Retinitis, Eye Retraction Syndrome, FA1, FAA, Fabry Disease, FAC, FACB, FACD, FACE, FACF, FACG, FACH, Facial Nerve Palsy, Facial Paralysis, Facial Ectodermal Dysplasias, Facial Ectodermal Dysplasia, Facio-Scapulo-Humeral Dystrophy, Facio-Auriculo-Vertebral Spectrum, Facio-cardio-cutaneous syndrome, Facio-Fronto-Nasal Dysplasia, Faciocutaneoskeletal Syndrome, Faciodigitogenital syndrome, Faciogenital dysplasia, Faciogenitopopliteal Syndrome, Faciopalatoosseous Syndrome, Faciopalatoosseous Syndrome Type II, Facioscapulohumeral muscular dystrophy, Factitious Hypoglycemia, Factor VIII Deficiency, Factor IX Deficiency, Factor XI Deficiency, Factor XII deficiency, Factor XIII Deficiency, Fahr Disease, Fahr's Disease, Failure of Secretion Gastric Intrinsic Factor, Fairbank Disease, Fallot's Tetralogy, Familial Acrogeria, Familial Acromicria, Familial Adenomatous Colon Polyposis, Familial Adenomatous Polyposis with Extraintestinal Manifestations, Familial Alobar Holoprosencephaly, Familial Alpha-Lipoprotein Deficiency, Familial Amyotrophic Chorea with Acanthocytosis, Familial Arrhythmic Myoclonus, Familial Articular Chondrocalcinosis, Familial Atypical Mole-Malignant Melanoma Syndrome, Familial Broad Beta Disease, Familial Calcium Gout, Familial Calcium Pyrophosphate Arthropathy, Familial Chronic Obstructive Lung Disease, Familial Continuous Skin Peeling, Familial Cutaneous Amyloidosis, Familial Dysproteinemia, Familial Emphysema, Familial Enteropathy Microvillus, Familial Foveal Retinoschisis, Familial Hibernation Syndrome, Familial High Cholesterol, Familial Hemochromatosis, Familial High Blood Cholesterol, Familial High-Density Lipoprotein Deficiency, Familial High Serum Cholesterol, Familial Hyperlipidema, Familial Hypoproteinemia with Lymphangietatic Enteropathy, Familial Jaundice, Familial Juvenile Nephronophtisis-Associated Ocular Anomaly, Familial Lichen Amyloidosis (Type IX), Familial Lumbar Stenosis, Familial Lymphedema Praecox, Familial Mediterranean Fever, Familial Multiple Polyposis,

Familial Nuchal Bleb, Familial Paroxysmal Polyserositis, Familial Polyposis Coli, Familial Primary Pulmonary Hypertension, Familial Renal Glycosuria, Familial Splenic Anemia, Familial Startle Disease, Familial Visceral Amyloidosis (Type VIII), FAMMM, FANCA, FANCB, FANCC, FANCD, FANCE, Fanconi Panmyelopathy, Fanconi Pancytopenia, Fanconi II, Fanconi's Anemia, Fanconi's Anemia Type I, Fanconi's Anemia Complementation Group, Fanconi's Anemia Complementation Group A, Fanconi's Anemia Complementation Group B, Fanconi's Anemia Complementation Group C, Fanconi's Anemia Complementation Group D, Fanconi's Anemia Complementation Group E, Fanconi's Anemia Complementation Group G, Fanconi's Anemia Complementation Group H, Fanconi's Anemia Estren-Dameshek Variant, FANF, FANG, FANH, FAP, FAPG, Farber's Disease, Farber's Lipogranulomatosis, FAS, Fasting Hypoglycemia, Fat-Induced Hyperlipemia, Fatal Granulomatous Disease of Childhood, Fatty Oxidation Disorders, Fatty Liver with Encephalopathy, FAV, FCH, FCMD, FCS Syndrome, FD, FDH, Febrile Mucocutaneous Syndrome Stevens Johnson Type, Febrile Neutrophilic Dermatosis Acute, Febrile Seizures, Feinberg's syndrome, Feissinger-Leroy-Reiter Syndrome, Female Pseudo-Turner Syndrome, Femoral Dysgenesis Bilateral-Robin Anomaly, Femoral Dysgenesis Bilateral, Femoral Facial Syndrome, Femoral Hypoplasia-Unusual Facies Syndrome, Fetal Alcohol Syndrome, Fetal Anti-Convulsant Syndrome, Fetal Cystic Hygroma, Fetal Effects of Alcohol, Fetal Effects of Chickenpox, Fetal Effects of Thalidomide, Fetal Effects of Varicella Zoster Virus, Fetal Endomyocardial Fibrosis, Fetal Face Syndrome, Fetal Iritis Syndrome, Fetal Transfusion Syndrome, Fetal Valproate Syndrome, Fetal Valproic Acid Exposure Syndrome, Fetal Varicella Infection, Fetal Varicella Zoster Syndrome, FFDD Type II, FG Syndrome, FGDY, FHS, Fibrin Stabilizing Factor Deficiency, Fibrinase Deficiency, Fibrinoid Degeneration of Astrocytes, Fibrinoid Leukodystrophy, Fibrinoligase Deficiency, Fibroblastoma Perineural, Fibrocystic Disease of Pancreas, Fibrodysplasia Ossificans Progressiva, Fibroelastic Endocarditis, Fibromyalgia, Fibromyalgia-Fibromyositis, Fibromyositis, Fibrosing Cholangitis, Fibrositis, Fibrous Ankylosis of Multiple Joints, Fibrous Cavernositis, Fibrous Dysplasia, Fibrous Plaques of the Penis, Fibrous Sclerosis of the Penis, Fickler-Winkler Type, Fiedler Disease, Fifth Digit Syndrome, Filippi Syndrome, Finnish Type Amyloidosis (Type V), First Degree Congenital Heart Block, First and Second Branchial Arch Syndrome,

Fischer's Syndrome, Fish Odor Syndrome, Fissured Tongue, Flat Adenoma Syndrome, Flatau-Schilder Disease, Flavin Containing Monooxygenase 2, Floating Beta Disease, Floating-Harbor Syndrome, Floating Spleen, Floppy Infant Syndrome, Floppy Valve Syndrome, Fluent aphasia, FMD, FMF, FMO Adult Liver Form, FMO2, FND, Focal Dermal Dysplasia Syndrome, Focal Dermal Hypoplasia, Focal Dermato-Phalangeal Dysplasia, Focal Dystonia, Focal Epilepsy, Focal Facial Dermal Dysplasia Type II, Focal Neuromyotonia, FODH, Folling Syndrome, Fong Disease, FOP, Forbes Disease, Forbes-Albright Syndrome, Forestier's Disease, Forsius-Eriksson Syndrome (X-Linked), Fothergill Disease, Fountain Syndrome, Foveal Dystrophy Progressive, FPO Syndrome Type II, FPO, Fraccaro Type Achondrogenesis (Type IB), Fragile X syndrome, Franceschetti-Zwalen-Klein Syndrome, Francois Dyscephaly Syndrome, Francois-Neetens Speckled Dystrophy, Flecked Corneal Dystrophy, Fraser Syndrome, FRAXA, FRDA, Fredrickson Type I Hyperlipoproteinemia, Freeman-Sheldon Syndrome, Freire-Maia Syndrome, Frey's Syndrome, Friedreich's Ataxia, Friedreich's Disease, Friedreich's Tabes, FRNS, Froelich's Syndrome, Frommel-Chiari Syndrome Lactation-Uterus Atrophy, Frontodigital Syndrome, Frontofacionasal Dysostosis, Frontofacionasal Dysplasia, Frontonasal Dysplasia, Frontonasal Dysplasia with Coronal Craniosynostosis, Fructose-1-Phosphate Aldolase Deficiency, Fructosemia, Fructosuria, Fryns Syndrome, FSH, FSHD, FSS, Fuchs Dystrophy, Fucosidosis Type 1, Fucosidosis Type 2, Fucosidosis Type 3, Fukuhara Syndrome, Fukuyama Disease, Fukuyama Type Muscular Dystrophy, Fumarylacetoacetase deficiency, Furrowed Tongue, G Syndrome, G6PD Deficiency, G6PD, GA I, GA IIB, GA IIA, GA II, GAII & MADD, Galactorrhea-Amenorrhea Syndrome Nonpuerperal, Galactorrhea-Amenorrhea without Pregnancy, Galactosamine-6-Sulfatase Deficiency, Galactose-1-Phosphate Uridyl Transferase Deficiency, Galactosemia, GALB Deficiency, Galloway-Mowat Syndrome, Galloway Syndrome, GALT Deficiency, Gammaglobulin Deficiency, GAN, Ganglioside Neuraminidase Deficiency, Ganglioside Sialidase Deficiency, Gangliosidosis GM1 Type 1, Gangliosidosis GM2 Type 2, Gangliosidosis Beta Hexosaminidase B Defeciency, Gardner Syndrome, Gargoylism, Garies-Mason Syndrome, Gasser Syndrome, Gastric Intrinsic Factor Failure of Secretion, Enterocyte Cobalamin, Gastrinoma, Gastritis, Gastroesophageal Laceration-Hemorrhage, Gastrointestinal Polyposis and Ectodermal Changes, Gastroschisis, Gaucher

Disease, Gaucher-Schlagenhaufer, Gayet-Wernicke Syndrome, GBS, GCA, GCM Syndrome, GCPS, Gee-Herter Disease, Gee-Thaysen Disease, Gehrig's Disease, Gelineau's Syndrome, Genee-Wiedemann Syndrome, Generalized Dystonia, Generalized Familial Neuromyotonia, Generalized Fibromatosis, Generalized Flexion Epilepsy, Generalized Glycogenosis, Generalized Hyperhidrosis, Generalized Lipofuscinosis, Generalized Myasthenia Gravis, Generalized Myotonia, Generalized Sporadic Neuromytonia, Genetic Disorders, Genital Defects, Genital and Urinary Tract Defects, Gerstmann Syndrome, Gerstmann Tetrad, GHBP, GHD, GHR, Giant Axonal Disease, Giant Axonal Neuropathy, Giant Benign Lymphoma, Giant Cell Glioblastoma Astrocytoma, Giant Cell Arteritis, Giant Cell Disease of the Liver, Giant Cell Hepatitis, Giant Cell of Newborns Cirrhosis, Giant Cyst of the Retina, Giant Lymph Node Hyperplasia, Giant Platelet Syndrome Hereditary, Giant Tongue, gic Macular Dystrophy, Gilbert's Disease, Gilbert Syndrome, Gilbert-Dreyfus Syndrome, Gilbert-Dreyfus Syndrome, Gilbert-Lereboullet Syndrome, Gilford Syndrome, Gilles de la Tourette's syndrome, Gillespie Syndrome, Gingival Fibromatosis-Abnormal Fingers Nails Nose Ear Splenomegaly, GLA Deficiency, GLA, GLB1, Glioma Retina, Global aphasia, Globoid Leukodystrophy, Glossoptosis Micrognathia and Cleft Palate, Glucocerebrosidase deficiency, Glucocerebrosidosis, Glucose-6-Phosphate Dehydrogenase Deficiency, Glucose-6-Phosphate Tranport Defect, Glucose-6-Phospate Translocase Deficiency, Glucose-G-Phosphatase Deficiency, Glucose-Galactose Malabsorption, Glucosyl Ceramide Lipidosis, Glutaric Aciduria I, Glutaric Acidemia I, Glutaric Acidemia II, Glutaric Aciduria II, Glutaric Aciduria Type II, Glutaric Aciduria Type III, Glutaricacidemia I, Glutaricacidemia II, Glutaricaciduria I, Glutaricaciduria II, Glutaricaciduria Type IIA, Glutaricaciduria Type IIB, Glutaryl-CoA Dehydrogenase Deficiency, Glutaurate-Aspartate Transport Defect, Gluten-Sensitive Enteropathy, Glycogen Disease of Muscle Type VII, Glycogen Storage Disease I, Glycogen Storage Disease III, Glycogen Storage Disease IV, Glycogen Storage Disease Type V, Glycogen Storage Disease VI, Glycogen Storage Disease VII, Glycogen Storage Disease VIII, Glycogen Storage Disease-Type II, Glycogenosis, Glycogenosis Type I, Glycogenosis Type IA, Glycogenosis Type IB, Glycogenosis Type II, Glycogenosis Type III, Glycogenosis Type IV, Glycogenosis Type V, Glycogenosis Type VI, Glycogenosis Type

VII, Glycogenosis Type VIII, Glycolic Aciduria, Glycolipid Lipidosis, GM2 Gangliosidosis Type 1, GM2 Gangliosidosis Type 1, GNPTA, Goitrous Autoimmune Thyroiditis, Goldenhar Syndrome, Goldenhar-Gorlin Syndrome, Goldscheider's Disease, Goltz Syndrome, Goltz-Gorlin Syndrome, Gonadal Dysgenesis 45 X, Gonadal Dysgenesis XO, Goniodysgenesis-Hypodontia, Goodman Syndrome, Goodman, Goodpasture Syndrome, Gordon Syndrome, Gorlin's Syndrome, Gorlin-Chaudhry-Moss Syndrome, Gottron Erythrokeratodermia Congenitalis Progressiva Symmetrica, Gottron's Syndrome, Gougerot-Carteaud Syndrome, Grand Mal Epilepsy, Granular Type Corneal Dystrophy, Granulomatous Arteritis, Granulomatous Colitis, Granulomatous Dermatitis with Eosinophilia, Granulomatous Ileitis, Graves Disease, Graves' Hyperthyroidism, Graves' Disease, Greig Cephalopolysyndactyly Syndrome, Groenouw Type I Corneal Dystrophy, Groenouw Type II Corneal Dystrophy, Gronblad-Strandberg Syndrome, Grotton Syndrome, Growth Hormone Receptor Deficiency, Growth Hormone Binding Protein Deficiency, Growth Hormone Deficiency, Growth-Mental Deficiency Syndrome of Myhre, Growth Retardation-Rieger Anomaly, GRS, Gruber Syndrome, GS, GSD6, GSD8, GTS, Guanosine Triphosphate-Cyclohydrolase Deficiency, Guanosine Triphosphate-Cyclohydrolase Deficiency, Guenther Porphyria, Guerin-Stern Syndrome, Guillain-Barré, Guillain-Barre Syndrome, Gunther Disease, H Disease, H. Gottron's Syndrome, Habit Spasms, HAE, Hageman Factor Deficiency, Hageman factor, Haim-Munk Syndrome, Hajdu-Cheney Syndrome, Hajdu Cheney, HAL Deficiency, Hall-Pallister Syndrome, Hallermann-Streiff-Francois syndrome, Hallermann-Streiff Syndrome, Hallervorden-Spatz Disease, Hallervorden-Spatz Syndrome, Hallopeau-Siemens Disease, Hallux Duplication Postaxial Polydactyly and Absence of Corpus Callosum, Halushi-Behcet's Syndrome, Hamartoma of the Lymphatics, Hand-Schueller-Christian Syndrome, HANE, Hanhart Syndrome, Happy Puppet Syndrome, Harada Syndrome, HARD +/-E Syndrome, HARD Syndrome, Hare Lip, Harlequin Fetus, Harlequin Type DOC 6, Harlequin Type Ichthyosis, Harley Syndrome, Harrington Syndrome, Hart Syndrome, Hartnup Disease, Hartnup Disorder, Hartnup Syndrome, Hashimoto's Disease, Hashimoto-Pritzker Syndrome, Hashimoto's Syndrome, Hashimoto's Thyroiditis, Hashimoto-Pritzker Syndrome, Hay Well's Syndrome, Hay-Wells Syndrome of Ectodermal Dysplasia, HCMM, HCP, HCTD, HD, Heart-Hand Syndrome (Holt-Oram Type), Heart Disease, Hecht Syndrome, HED,

Heerferdt-Waldenstrom and Lofgren's Syndromes, Hegglin's Disease, Heinrichsbauer Syndrome, Hemangiomas, Hemangioma Familial, Hemangioma-Thrombocytopenia Syndrome, Hemangiomatosis Chondrodystrophica, Hemangiomatous Branchial Clefts-Lip Pseudocleft Syndrome, Hemifacial Microsomia, Hemimegalencephaly, Hemiparesis of Cerebral Palsy, Hemiplegia of Cerebral Palsy, Hemisection of the Spinal Cord, Hemochromatosis, Hemochromatosis Syndrome, Hemodialysis-Related Amyloidosis, Hemoglobin Lepore Syndromes, Hemolytic Anemia of Newborn, Hemolytic Cold Antibody Anemia, Hemolytic Disease of Newborn, Hemolytic-Uremic Syndrome, Hemophilia, Hemophilia A, Hemophilia B, Hemophilia B Factor IX, Hemophilia C, Hemorrhagic Dystrophic Thrombocytopenia, Hemorrhagica Aleukia, Hemosiderosis, Hepatic Fructokinase Deficiency, Hepatic Phosphorylase Kinase Deficiency, Hepatic Porphyria, Hepatic Porphyrias, Hepatic Veno-Occlusive Diseas, Hepato-Renal Syndrome, Hepatolenticular Degeneration, Hepatophosphorylase Deficiency, Hepatorenal Glycogenosis, Hepatorenal Syndrome, Hepatorenal Tyrosinemia, Hereditary Acromelalgia, Hereditary Alkaptonuria, Hereditary Amyloidosis, Hereditary Angioedema, Hereditary Areflexic Dystasia, Heredopathia Atactica Polyneuritiformis, Hereditary Ataxia, Hereditary Ataxia Friedrich's Type, Hereditary Benign Acanthosis Nigricans, Hereditary Cerebellar Ataxia, Hereditary Chorea, Hereditary Chronic Progressive Chorea, Hereditary Connective Tissue Disorders, Hereditary Coproporphyria, Hereditary Coproporphyria Porphyria, Hereditary Cutaneous Malignant Melanoma, Hereditary Deafness-Retinitis Pigmentosa, Heritable Disorder of Zinc Deficiency, Hereditary DNS, Hereditary Dystopic Lipidosis, Hereditary Emphysema, Hereditary Fructose Intolerance, Hereditary Hemorrhagic Telangiectasia, Hereditary Hemorrhagic Telangiectasia Type I, Hereditary Hemorrhagic Telangiectasia Type II, Hereditary Hemorrhagic Telangiectasia Type III, Hereditary Hyperuricemia and Choreoathetosis Syndrome, Hereditary Leptocytosis Major, Hereditary Leptocytosis Minor, Hereditary Lymphedema, Hereditary Lymphedema Tarda, Hereditary Lymphedema Type I, Hereditary Lymphedema Type II, Hereditary Motor Sensory Neuropathy, Hereditary Motor Sensory Neuropathy I, Hereditary Motor Sensory Neuropathy Type III, Hereditary Nephritis, Hereditary Nephritis and Nerve Deafness, Hereditary Nephropathic Amyloidosis, Hereditary Nephropathy and Deafness, Hereditary Nonpolyposis Colorectal Cancer, Hereditary Nonpolyposis

Colorectal Carcinoma, Hereditary Nonspherocytic Hemolytic Anemia, Hereditary Onychoosteodysplasia, Hereditary Optic Neuroretinopathy, Hereditary Polyposis Coli, Hereditary Sensory and Autonomic Neuropathy Type I, Hereditary Sensory and Autonomic Neuropathy Type II, Hereditary Sensory and Autonomic Neuropathy Type III, Hereditary Sensory Motor Neuropathy, Hereditary Sensory Neuropathy Type I, Hereditary Sensory Neuropathy Type II, Hereditary Sensory Neuropathy Type III, Hereditary Sensory Radicular Neuropathy Type I, Hereditary Sensory Radicular Neuropathy Type II, Hereditary Site Specific Cancer, Hereditary Spherocytic Hemolytic Anemia, Hereditary Spherocytosis, Hereditary Tyrosinemia Type 1, Heritable Connective Tissue Disorders, Herlitz Syndrome, Hermans-Herzberg Phakomatosis, Hermansky-Pudlak Syndrome, Hermansky-Pudlak Syndrome, Hermaphroditism, Herpes Zoster, Herpes Iris Stevens-Johnson Type, Hers Disease, Heterozygous Beta Thalassemia, Hexoaminidase Alpha-Subunit Deficiency (Variant B), Hexoaminidase Alpha-Subunit Deficiency (Variant B), HFA, HFM, HGPS, HH, HHHO, HHRH, HHT, Hiatal Hernia-Microcephaly-Nephrosis Galloway Type, Hidradenitis Suppurativa, Hidrosadenitis Axillaris, Hidrosadenitis Suppurativa, Hidrotic Ectodermal Dysplasias, HIE Syndrome, High Imperforate Anus, High Potassium, High Scapula, HIM, Hirschsprung's Disease, Hirschsprung's Disease Acquired, Hirschsprung Disease Polydactyly of Ulnar & Big Toe and VSD, Hirschsprung Disease with Type D Brachydactyly, Hirsutism, HIS Deficiency, Histidine Ammonia-Lyase (HAL) Deficiency, Histidase Deficiency, Histidinemia, Histiocytosis, Histiocytosis X, HLHS, HLP Type II, HMG, HMI, HMSN I, HNHA, HOCM, Hodgkin Disease, Hodgkin's Disease, Hodgkin's Lymphoma, Hollaender-Simons Disease, Holmes-Adie Syndrome, Holocarboxylase Synthetase Deficiency, Holoprosencephaly, Holoprosencephaly Malformation Complex, Holoprosencephaly Sequence, Holt-Oram Syndrome, Holt-Oram Type Heart-Hand Syndrome, Homocystinemia, Homocystinuria, Homogentisic Acid Oxidase Deficiency, Homogentisic Acidura, Homozygous Alpha-1-Antitrypsin Deficiency, HOOD, Horner Syndrome, Horton's disease, HOS, HOS1, Houston-Harris Type Achrondrogenesis (Type IA), HPS, HRS, HS, HSAN Type I, HSAN Type II, HSAN-III, HSMN, HSMN Type III, HSN I, HSN-III, Huebner-Herter Disease, Hunner's Patch, Hunner's Ulcer, Hunter Syndrome, Hunter-Thompson Type Acromesomelic Dysplasia, Huntington's Chorea, Huntington's Disease, Hurler Disease,

Hurler Syndrome, Hurler-Scheie Syndrome, HUS, Hutchinson-Gilford Progeria Syndrome, Hutchinson-Gilford Syndrome, Hutchinson-Weber-Peutz Syndrome, Hutterite Syndrome Bowen-Conradi Type, Hyaline Panneuropathy, Hydranencephaly, Hydrocephalus, Hydrocephalus Agyria and Retinal Dysplasia, Hydrocephalus Internal Dandy-Walker Type, Hydrocephalus Noncommunicating Dandy-Walker Type, Hydrocephaly, Hydronephrosis With Peculiar Facial Expression, Hydroxylase Deficiency, Hygroma Colli, Hyper-IgE Syndrome, Hyper-IgM Syndrome, Hyper IgM Syndrome, Hyperaldosteronism, Hyperaldosteronism With Hypokalemic Alkatosis, Hyperaldosteronism Without Hypertension, Hyperammonemia, Hyperammonemia Due to Carbamylphosphate Synthetase Deficiency, Hyperammonemia Due to Ornithine Transcarbamylase Deficiency, Hyperammonemia Type II, Hyper-Beta Carnosinemia, Hyperbilirubinemia I, Hyperbilirubinemia II, Hypercalcemia Familial with Nephrocalcinosis and Indicanuria, Hypercalcemia-Supravalvar Aortic Stenosis, Hypercalciuric Rickets, Hypercapnic acidosis, Hypercatabolic Protein-Losing Enteropathy, Hyperchloremic acidosis, Hypercholesterolemia, Hypercholesterolemia Type IV, Hyperchylomicronemia, Hypercystinuria, Hyperekplexia, Hyperextensible joints, Hyperglobulinemic Purpura, Hyperglycinemia with Ketoacidosis and Lactic Acidosis Propionic Type, Hyperglycinemia Nonketotic, Hypergonadotropic Hypogonadism, Hyperimmunoglobulin E Syndrome, Hyperimmunoglobulin E-Recurrent Infection Syndrome, Hyperimmunoglobulinemia E-Staphylococcal, Hyperkalemia, Hyperkinetic Syndrome, Hyperlipemic Retinitis, Hyperlipidemia I, Hyperlipidemia IV, Hyperlipoproteinemia Type I, Hyperlipoproteinemia Type III, Hyperlipoproteinemia Type IV, Hyperoxaluria, Hyperphalangy-Clinodactyly of Index Finger with Pierre Robin Syndrome, Hyperphenylalanemia, Hyperplastic Epidermolysis Bullosa, Hyperpnea, Hyperpotassemia, Hyperprebeta-Lipoproteinemia, Hyperprolinemia Type I, Hyperprolinemia Type II, Hypersplenism, Hypertelorism with Esophageal Abnormalities and Hypospadias, Hypertelorism-Hypospadias Syndrome, Hypertrophic Cardiomyopathy, Hypertrophic Interstitial Neuropathy, Hypertrophic Interstitial Neuritis, Hypertrophic Interstitial Radiculoneuropathy, Hypertrophic Neuropathy of Refsum, Hypertrophic Obstructive Cardiomyopathy, Hyperuricemia Choreoathetosis Self-multilation Syndrome, Hyperuricemia-Oligophrenia, Hypervalinemia, Hypocalcified (Hypomineralized) Type, Hypochondrogenesis,

Hypochrondroplasia, Hypogammaglobulinemia, Hypogammaglobulinemia Transient of Infancy, Hypogenital Dystrophy with Diabetic Tendency, Hypoglossia-Hypodactylia Syndrome, Hypoglycemia, Exogenous Hypoglycemia, Hypoglycemia with Macroglossia, Hypoglycosylation Syndrome Type 1a, Hypogonadism with Anosmia, Hypogonadotropic Hypogonadism and Anosmia, Hypohidrotic Ectodermal Dysplasia, Hypohidrotic Ectodermal Dysplasia Autosomal Dominant type, Hypohidrotic Ectodermal Dysplasias Autorecessive, Hypokalemia, Hypokalemic Alkalosis with Hypercalciuria, Hypokalemic Syndrome, Hypolactasia, Hypomaturation Type (Snow-Capped Teeth), Hypomelanosis of Ito, Hypomelia-Hypotrichosis-Facial Hemangioma Syndrome, Hypomyelination Neuropathy, Hypoparathyroidism, Hypophosphatasia, Hypophosphatemic Rickets with Hypercalcemia, Hypopigmentation, Hypopigmented macular lesion, Hypoplasia of the Depressor Anguli Oris Muscle with Cardiac Defects, Hypoplastic Anemia, Hypoplastic Congenital Anemia, Hypoplastic Chondrodystrophy, Hypoplastic Enamel-Onycholysis-Hypohidrosis, Hypoplastic (Hypoplastic-Explastic) Type, Hypoplastic Left Heart Syndrome, Hypoplastic-Triphalangeal Thumbs, Hypopotassemia Syndrome, Hypospadias-Dysphagia Syndrome, Hyposmia, Hypothalamic Hamartoblastoma Hypopituitarism Imperforate Anus Polydactyly, Hypothalamic Infantilism-Obesity, Hypothyroidism, Hypotonia-Hypomentia-Hypogonadism-Obesity Syndrome, Hypoxanthine-Guanine Phosphoribosyltranferase Defect (Complete Absense of), I-Cell Disease, Iatrogenic Hypoglycemia, IBGC, IBIDS Syndrome, IBM, IBS, IC, I-Cell Disease, ICD, ICE Syndrome Cogan-Reese Type, Icelandic Type Amyloidosis (Type VI), I-Cell Disease, Ichthyosiform Erythroderma Corneal Involvement and Deafness, Ichthyosiform Erythroderma Hair Abnormality Growth and Men, Ichthyosiform Erythroderma with Leukocyte Vacuolation, Ichthyosis, Ichthyosis Congenita, Ichthyosis Congenital with Trichothiodystrophy, Ichthyosis Hystrix, Ichthyosis Hystrix Gravior, Ichthyosis Linearis Circumflexa, Ichthyosis Simplex, Ichthyosis Tay Syndrome, Ichthyosis Vulgaris, Ichthyotic Neutral Lipid Storage Disease, Icteric Leptospirosis, Icterohemorrhagic Leptospirosis, Icterus (Chronic Familial), Icterus Gravis Neonatorum, Icterus Intermittens Juvenalis, Idiopathic Alveolar Hypoventilation, Idiopathic Amyloidosis, Idiopathic Arteritis of Takayasu, Idiopathic Basal Ganglia Calcification (IBGC), Idiopathic Brachial Plexus Neuropathy, Idiopathic Cervical Dystonia, Idiopathic Dilatation of the Pulmonary

Artery, Idiopathic Facial Palsy, Idiopathic Familial Hyperlipemia, Idiopathic Hypertrophic Subaortic Stenosis, Idiopathic Hypoproteinemia, Idiopathic Immunoglobulin Deficiency, Idiopathic Neonatal Hepatitis, Idiopathic Non-Specific Ulcerative Colitis, Idiopathic Peripheral Periphlebitis, Idiopathic Pulmonary Fibrosis, Idiopathic Refractory Sideroblastic Anemia, Idiopathic Renal Hematuria, Idiopathic Steatorrhea, Idiopathic Thrombocythemia, Idiopathic Thrombocytopenic Purpura, Idiopathic Thrombocytopenia Purpura (ITP), IDPA, IgA Nephropathy, IHSS, Ileitis, Ileocolitis, Illinois Type Amyloidosis, ILS, IM, IMD2, IMD5, Immune Defect due to Absence of Thymus, Immune Hemolytic Anemia Paroxysmal Cold, Immunodeficiency with Ataxia Telangiectasia, Immunodeficiency Cellular with Abnormal Immunoglobulin Synthesis, Immunodeficiency Common Variable Unclassifiable, Immunodeficiency with Hyper-IgM, Immunodeficiency with Leukopenia, Immunodeficiency-2, Immunodeficiency-5 (IMD5), Immunoglobulin Deficiency, Imperforate Anus, Imperforate Anus with Hand Foot and Ear Anomalies, Imperforate Nasolacrimal Duct and Premature Aging Syndrome, Impotent Neutrophil Syndrome, Inability To Open Mouth Completely And Short Finger-Flexor, INAD, Inborn Error of Urea Synthesis Arginase Type, Inborn Error of Urea Synthesis Arginino Succinic Type, Inborn Errors of Urea Synthesis Carbamyl Phosphate Type, Inborn Error of Urea Synthesis Citrullinemia Type, Inborn Errors of Urea Synthesis Glutamate Synthetase Type, INCL, Inclusion body myositis, Incomplete Atrioventricular Septal Defect, Incomplete Testicular Feminization, Incontinentia Pigmenti, Incontinenti Pigmenti Achromians, Index Finger Anomaly with Pierre Robin Syndrome, Indiana Type Amyloidosis (Type II), Indolent systemic mastocytosis, Infantile Acquired Aphasia, Infantile Autosomal Recessive Polycystic Kidney Disease, Infantile Beriberi, Infantile Cerebral Ganglioside, Infantile Cerebral Ganglioside, Infantile Cerebral Paralysis, Infantile Cystinosis, Infantile Epileptic, Infantile Fanconi Syndrome with Cystinosis, Infantile Finnish Type Neuronal Ceroid Lipofuscinosis, Infantile Gaucher Disease, Infantile Hypoglycemia, Infantile Hypophasphatasia, Infantile Lobar Emphysema, Infantile Myoclonic Encephalopathy, Infantile Myoclonic Encephalopathy and Polymyoclonia, Infantile Myofibromatosis, Infantile Necrotizing Encephalopathy, Infantile Neuronal Ceroid Lipofuscinosis, Infantile Neuroaxonal Dystrophy, Infantile Onset Schindler Disease, Infantile Phytanic Acid Storage Disease, Infantile Refsum Disease (IRD), Infantile Sipoidosis GM-2

Gangliosideosis (Type S), Infantile Sleep Apnea, Infantile Spasms, Infantile Spinal Muscular Atrophy (all types), Infantile Spinal Muscular Atrophy ALS, Infantile Spinal Muscular Atrophy Type I, Infantile Type Neuronal Ceroid Lipofuscinosis, Infectious Jaundice, Inflammatory Breast Cancer, Inflammatory Linear Nevus Sebaceous Syndrome, Iniencephaly, Insulin Resistant Acanthosis Nigricans, Insulin Lipodystrophy, Insulin dependent Diabetes, Intention Myoclonus, Intermediate Cystinosis, Intermediate Maple Syrup Urine Disease, Intermittent Ataxia with Pyruvate Dehydrogenase Deficiency, Intermittent Maple Syrup Urine Disease, Internal Hydrocephalus, Interstitial Cystitis, Interstitial Deletion of 4q Included, Intestinal Lipodystrophy, Intestinal Lipophagic Granulomatosis, Intestinal Lymphangiectasia, Intestinal Polyposis I, Intestinal Polyposis II, Intestinal Polyposis III, Intestinal Polyposis-Cutaneous Pigmentation Syndrome, Intestinal Pseudoobstruction with External Ophthalmoplegia, Intracranial Neoplasm, Intracranial Tumors, Intracranial Vascular Malformations, Intrauterine Dwarfism, Intrauterine Synechiae, Inverted Smile And Occult Neuropathic Bladder, Iowa Type Amyloidosis (Type IV), IP, IPA, Iridocorneal Endothelial Syndrome, Iridocorneal Endothelial (ICE) Syndrome Cogan-Resse Type, Iridogoniodysgenesis With Somatic Anomalies, Iris Atrophy with Corneal Edema and Glaucoma, Iris Nevus Syndrome, Iron Overload Anemia, Iron Overload Disease, Irritable Bowel Syndrome, Irritable Colon Syndrome, Isaacs Syndrome, Isaacs-Merten Syndrome, Ischemic Cardiomyopathy, Isolated Lissencephaly Sequence, Isoleucine 33 Amyloidosis, Isovaleric Acid CoA Dehydrogenase Deficiency, Isovaleric Acidaemia, Isovalericacidemia, Isovaleryl CoA Carboxylase Deficiency, ITO Hypomelanosis, ITO, ITP, IVA, Ivemark Syndrome, Iwanoff Cysts, Jackknife Convulsion, Jackson-Weiss Craniosynostosis, Jackson-Weiss Syndrome, Jacksonian Epilepsy, Jacobsen Syndrome, Jadassohn-Lewandowsky Syndrome, Jaffe-Lichenstein Disease, Jakob's Disease, Jakob-Creutzfeldt Disease, Janeway I, Janeway Dysgammaglobulinemia, Jansen Metaphyseal Dysostosis, Jansen Type Metaphyseal Chondrodysplasia, Jarcho-Levin Syndrome, Jaw-Winking, JBS, JBS, JDMS, Jegher's Syndrome, Jejunal Atresia, Jejunitis, Jejunoileitis, Jervell and Lange-Nielsen Syndrome, Jeune Syndrome, JMS, Job Syndrome, Job-Buckley Syndrome, Johanson-Blizzard Syndrome, John Dalton, Johnson-Stevens Disease, Jonston's Alopecia, Joseph's Disease, Joseph's Disease Type I, Joseph's Disease Type II, Joseph's Disease Type III, Joubert

Syndrome, Joubert-Bolthauser Syndrome, JRA, Juberg Hayward Syndrome, Juberg-Marsidi Syndrome, Juberg-Marsidi Mental Retardation Syndrome, Jumping Frenchmen, Jumping Frenchmen of Maine, Juvenile Arthritis, Juvenile Autosomal Recessive Polycystic Kidney Disease, Juvenile Cystinosis, Juvenile (Childhood) Dermatomyositis (JDMS), Juvenile Diabetes, Juvenile Gaucher Disease, Juvenile Gout Choreoathetosis and Mental Retardation Syndrome, Juvenile Intestinal Malabsorption of Vit B12, Juvenile Intestinal Malabsorption of Vitamin B12, Juvenile Macular Degeneration, Juvenile Pernicious Anemia, Juvenile Retinoschisis, Juvenile Rheumatoid Arthritis, Juvenile Spinal Muscular Atrophy Included, Juvenile Spinal Muscular Atrophy ALS Included, Juvenile Spinal Muscular Atrophy Type III, Juxta-Articular Adiposis Dolorosa, Juxtaglomerular Hyperplasia, Kabuki Make-Up Syndrome, Kahler Disease, Kallmann Syndrome, Kanner Syndrome, Kanzaki Disease, Kaposi Disease (not Kaposi Sarcoma), Kappa Light Chain Deficiency, Karsch-Neugebauer Syndrome, Kartagener Syndrome-Chronic Sinobronchial Disease and Dextrocardia, Kartagener Triad, Kasabach-Merritt Syndrome, Kast Syndrome, Kawasaki Disease, Kawasaki Syndrome, KBG Syndrome, KD, Kearns-Sayre Disease, Kearns-Sayre Syndrome, Kennedy Disease, Kennedy Syndrome, Kennedy Type Spinal and Bulbar Muscular Atrophy, Kennedy-Stefanis Disease, Kenny Disease, Kenny Syndrome, Kenny Type Tubular Stenosis, Kenny-Caffe Syndrome, Kera. Palmoplant. Con. Pes Planus Ony. Periodon. Arach., Keratitis Ichthyosis Deafness Syndrome, Keratoconus, Keratoconus Posticus Circumscriptus, Keratolysis, Keratolysis Exfoliativa Congenita, Keratolytic Winter Erythema, Keratomalacia, Keratosis Follicularis, Keratosis Follicularis Spinulosa Decalvans, Keratosis Follicularis Spinulosa Decalvans Ichthyosis, Keratosis Nigricans, Keratosis Palmoplantaris with Periodontopathia and Onychogryposis, Keratosis Palmoplantaris Congenital Pes Planus Onychogryposis Periodontosis Arachnodactyly, Keratosis Palmoplantaris Congenital, Pes Planus, Onychogryphosis, Periodontosis, Arachnodactyly, Acroosteolysis, Keratosis Rubra Figurata, Keratosis Seborrheica, Ketoacid Decarboxylase Deficiency, Ketoaciduria, Ketotic Glycinemia, KFS, KID Syndrome, Kidney Agenesis, Kidneys Cystic-Retinal Aplasia Joubert Syndrome, Killian Syndrome, Killian/Teschler-Nicola Syndrome, Kiloh-Nevin syndrome III, Kinky Hair Disease, Kinsbourne Syndrome, Kleeblattschadel Deformity, Kleine-Levin Syndrome, Kleine-Levin Hibernation Syndrome, Klinefelter, Klippel-Feil Syndrome, Klippel-Feil

Syndrome Type I, Klippel-Feil Syndrome Type II, Klippel-Feil Syndrome Type III, Klippel Trenaunay Syndrome, Klippel-Trenaunay-Weber Syndrome, Kluver-Bucy Syndrome, KMS, Kniest Dysplasia, Kniest Syndrome, Kobner's Disease, Koebberling-Dunnigan Syndrome, Kohlmeier-Degos Disease, Kok Disease, Korsakoff Psychosis, Korsakoff's Syndrome, Krabbe's Disease Included, Krabbe's Leukodystrophy, Kramer Syndrome, KSS, KTS, KTW Syndrome, Kufs Disease, Kugelberg-Welander Disease, Kugelberg-Welander Disease, Kugelberg-Welander Syndrome, Kussmaul-Landry Paralysis, KWS, L-3-Hydroxy-Acyl-CoA Dehydrogenase (LCHAD) Deficiency, Laband Syndrome, Labhart-Willi Syndrome, Labyrinthine Syndrome, Labyrinthine Hydrops, Lacrimo-Auriculo-Dento-Digital Syndrome, Lactase Isolated Intolerance, Lactase Deficiency, Lactation-Uterus Atrophy, Lactic Acidosis Leber Hereditary Optic Neuropathy, Lactic and Pyruvate Acidemia with Carbohydrate Sensitivity, Lactic and Pyruvate Acidemia with Episodic Ataxia and Weakness, Lactic and Pyruvate Acidemia with Carbohydrate Sensitivity,Lactic and Pyruvate, Lactic acidosis, Lactose Intolerance of Adulthood, Lactose Intolerance, Lactose Intolerance of Childhood, LADD Syndrome, LADD, Lafora Disease Included, Lafora Body Disease, Laki-Lorand Factor Deficiency, LAM, Lambert Type Ichthyosis, Lambert-Eaton Syndrome, Lambert-Eaton Myasthenic Syndrome, Lamellar Recessive Ichthyosis, Lamellar Ichthyosis, Lamellar Recessive Ichthyosis, Lancereaux-Mathieu-Weil Spirochetosis, Landau-Kleffner Syndrome, Landouzy Dejerine Muscular Dystrophy, Landry Ascending Paralysis, Langer-Salidino Type Achondrogensis (Type II), Langer Giedion Syndrome, Langerhans-Cell Granulomatosis, Langerhans-Cell Histiocytosis (LCH), Large Atrial and Ventricular Defect, Laron Dwarfism, Laron Type Pituitary Dwarfism, Larsen Syndrome, Laryngeal Dystonia, Latah (Observed in Malaysia), Late Infantile Neuroaxonal Dystrophy, Late Onset Cockayne Syndrome Type III (Type C), Late-Onset Dystonia, Late-Onset Immunoglobulin Deficiency, Late Onset Pelizaeus-Merzbacher Brain Sclerosis, Lattice Corneal Dystrophy, Lattice Dystrophy, Launois-Bensaude, Launois-Cleret Syndrome, Laurence Syndrome, Laurence-Moon Syndrome, Laurence-Moon/Bardet-Biedl, Lawrence-Seip Syndrome, LCA, LCAD Deficiency, LCAD, LCADH Deficiency, LCH, LCHAD, LCPD, Le Jeune Syndrome, Leband Syndrome, Leber's Amaurosis, Leber's Congenital Amaurosis,Congenital Absence of the Rods and Cones, Leber's Congenital Tapetoretinal

Degeneration, Leber's Congenital Tapetoretinal Dysplasia, Leber's Disease, Leber's Optic Atrophy, Leber's Optic Neuropathy, Left Ventricular Fibrosis, Leg Ulcer, Legg-Calve-Perthes Disease, Leigh's Disease, Leigh's Syndrome, Leigh's Syndrome (Subacute Necrotizing Encephalomyelopathy), Leigh Necrotizing Encephalopathy, Lennox-Gastaut Syndrome, Lentigio-Polypose-Digestive Syndrome, Lenz Dysmorphogenetic Syndrome, Lenz Dysplasia, Lenz Microphthalmia Syndrome, Lenz Syndrome, LEOPARD Syndrome, Leprechaunism, Leptomeningeal Angiomatosis, Leptospiral Jaundice, Leri-Weill Disease, Leri-Weil Dyschondrosteosis, Leri-Weil Syndrome, Lermoyez Syndrome, Leroy Disease, Lesch Nyhan Syndrome, Lethal Infantile Cardiomyopathy, Lethal Neonatal Dwarfism, Lethal Osteochondrodysplasia, Letterer-Siwe Disease, Leukocytic Anomaly Albinism, Leukocytic Inclusions with Platelet Abnormality, Leukodystrophy, Leukodystrophy with Rosenthal Fibers, Leukoencephalitis Periaxialis Concentric, Levine-Critchley Syndrome, Levulosuria, Levy-Hollister Syndrome, LGMD, LGS, LHON, LHON, LIC, Lichen Ruber Acuminatus, Lichen Acuminatus, Lichen Amyloidosis, Lichen Planus, Lichen Psoriasis, Lignac-Debre-Fanconi Syndrome, Lignac-Fanconi Syndrome, Ligneous Conjunctivitis, Limb-Girdle Muscular Dystrophy, Limb Malformations-Dento-Digital Syndrome, Limit Dextrinosis, Linear Nevoid Hypermelanosis, Linear Nevus Sebacous Syndrome, Linear Scleroderma, Linear Sebaceous Nevus Sequence, Linear Sebaceous Nevus Syndrome, Lingua Fissurata, Lingua Plicata, Lingua Scrotalis, Linguofacial Dyskinesia, Lip Pseudocleft-hemangiomatous Branchial Cyst Syndrome, Lipid Granulomatosis, Lipid Histiocytosis, Lipid Kerasin Type, Lipid Storage Disease, Lipid-Storage Myopathy Associated with SCAD Deficiency, Lipidosis Ganglioside Infantile, Lipoatrophic Diabetes Mellitus, Lipodystrophy, Lipoid Corneal Dystrophy, Lipoid Hyperplasia-Male Pseudohermaphroditism, Lipomatosis of Pancreas Congenital, Lipomucopolysaccharidosis Type I, Lipomyelomeningocele, Lipoprotein Lipase Deficiency Familial, LIS, LIS1, Lissencephaly 1, Lissencephaly Type I, Lissencephaly variants with agenesis of the corpus callosum cerebellar hypoplasia or other anomalies, Little Disease, Liver Phosphorylase Deficiency, LKS, LM Syndrome, Lobar Atrophy, Lobar Atrophy of the Brain, Lobar Holoprosencephaly, Lobar Tension Emphysema in Infancy, Lobstein Disease (Type I), Lobster Claw Deformity, Localized Epidermolysis Bullosa, Localized Lipodystrophy, Localized Neuritis of the Shoulder Girdle, Loeffler's Disease, Loeffler Endomyocardial

Fibrosis with Eosinophilia, Loeffler Fibroplastic Parietal Endocarditis, Loken Syndrome, Loken-Senior Syndrome, Long-Chain 3-hydroxyacyl-CoA Dehydrogenase (LCHAD), Long Chain Acyl CoA Dehydrogenase Deficiency, Long-Chain Acyl-CoA Dehydrogenase (ACADL), Long QT Syndrome without Deafness, Lou Gehrig's Disease, Lou Gehrig's Disease Included, Louis-Bar Syndrome, Low Blood Sugar, Low-Density Beta Lipoprotein Deficiency, Low Imperforate Anus, Low Potassium Syndrome, Lowe syndrome, Lowe's Syndrome, Lowe-Bickel Syndrome, Lowe-Terry-MacLachlan Syndrome, LS, LTD, Lubs Syndrome, Luft Disease, Lumbar Canal Stenosis, Lumbar Spinal Stenosis, Lumbosacral Spinal Stenosis, Lundborg-Unverricht Disease, Lundborg-Unverricht Disease Included, Lupus, Lupus Erythematosus, Luschka-Magendie Foramina Atresia, Lyell Syndrome, Lyelles Syndrome, Lymphadenoid Goiter, Lymphangiectatic Protein-Losing Enteropathy, Lymphangioleiomatosis, Lymphangioleimyomatosis, Lymphangiomas, Lymphatic Malformations, Lynch Syndromes, Lynch Syndrome I, Lynch Syndrome II, Lysosomal Alpha-N-Acetylgalactosaminidase Deficiency Schindler Type, Lysosomal Glycoaminoacid Storage Disease-Angiokeratoma Corporis Diffusum, Lysosomal Glucosidase Deficiency, MAA, Machado Disease, Machado-Joseph Disease, Macrencephaly, Macrocephaly, Macrocephaly Hemihypertrophy, Macrocephaly with Multiple Lipomas and Hemangiomata, Macrocephaly with Pseudopapilledema and Multiple Hemangiomata, Macroglobulinemia, Macroglossia, Macroglossia-Omphalocele-Visceromegaly Syndrome, Macrostomia Ablepheron Syndrome, Macrothrombocytopenia Familial Bernard-Soulier Type, Macula Lutea degeneration, Macular Amyloidosis, Macular Degeneration, Macular Degeneration Disciform, Macular Degeneration Senile, Macular Dystrophy, Macular Type Corneal Dystrophy, MAD, Madelung's Disease, Maffucci Syndrome, Major Epilepsy, Malabsorption, Malabsorption-Ectodermal Dysplasia-Nasal Alar Hypoplasia, Maladie de Roger, Maladie de Tics, Male Malformation of Limbs and Kidneys, Male Turner Syndrome, Malignant Acanthosis, Malignant Acanthosis Nigricans, Malignant Astrocytoma, Malignant Atrophic Papulosis, Malignant Fever, Malignant Hyperphenylalaninemia, Malignant Hyperpyrexia, Malignant Hyperthermia, Malignant Melanoma, Malignant Tumors of the Central Nervous System, Mallory-Weiss Laceration, Mallory-Weiss Tear, Mallory-Weiss Syndrome, Mammary Paget's Disease, Mandibular Ameloblastoma, Mandibulofacial Dysostosis, Mannosidosis,

Map-Dot-Fingerprint Type Corneal Dystrophy, Maple Syrup Urine Disease, Marble Bones, Marchiafava-Micheli Syndrome, Marcus Gunn Jaw-Winking Syndrome, Marcus Gunn Phenomenon, Marcus Gunn Ptosis with jaw-winking, Marcus Gunn Syndrome, Marcus Gunn (Jaw-Winking) Syndrome, Marcus Gunn Ptosis (with jaw-winking), Marden-Walker Syndrome, Marden-Walker Type Connective Tissue Disorder, Marfan's Abiotrophy, Marfan-Achard syndrome, Marfan Syndrome, Marfan's Syndrome I, Marfan's Variant, Marfan-Achard syndrome, Marfanoid Hypermobility Syndrome, Marginal Corneal Dystrophy, Marie's Ataxia, Marie's Ataxia, Marie Disease, Marie-Sainton Disease, Marie Strumpell Disease, Marie-Strumpell Spondylitis, Marinesco-Sjogren Syndrome, Marinesco-Sjogren-Gorland Syndrome, Marker X Syndrome, Maroteaux Lamy Syndrome, Maroteaux Type Acromesomelic Dysplasia, Marshall's Ectodermal Dysplasias With Ocular and Hearing Defects, Marshall-Smith Syndrome, Marshall Syndrome, Marshall Type Deafness-Myopia-Cataract-Saddle Nose, Martin-Albright Syndrome, Martin-Bell Syndrome, Martorell Syndrome, MASA Syndrome, Massive Myoclonia, Mast Cell Leukemia, Mastocytosis, Mastocytosis With an Associated Hematologic Disorder, Maumenee Corneal Dystrophy, Maxillary Ameloblastoma, Maxillofacial Dysostosis, Maxillonasal Dysplasia, Maxillonasal Dysplasia Binder Type, Maxillopalpebral Synkinesis, May-Hegglin Anomaly, MCAD Deficiency, MCAD, McArdle Disease, McCune-Albright, MCD, McKusick Type Metaphyseal Chondrodysplasia, MCR, MCTD, Meckel Syndrome, Meckel-Gruber Syndrome, Median Cleft Face Syndrome, Mediterranean Anemia, Medium-Chain Acyl-CoA dehydrogenase (ACADM), Medium Chain Acyl-CoA Dehydrogenase (MCAD) Deficiency, Medium-Chain Acyl-CoA Dehydrogenase Deficiency, Medium Chain Acyl CoA Dehydrogenase Deficiency, Medullary Cystic Disease, Medullary Sponge Kidney, MEF, Megaesophagus, Megalencephaly, Megalencephaly with Hyaline Inclusion, Megalencephaly with Hyaline Panneuropathy, Megaloblastic Anemia, Megaloblastic Anemia of Pregnancy, Megalocornea-Mental Retardation Syndrome, Meier-Gorlin Syndrome, Meige's Lymphedema, Meige's Syndrome, Melanodermic Leukodystrophy, Melanoplakia-Intestinal Polyposis, MELAS Syndrome, MELAS, Melkersson Syndrome, Melnick-Fraser Syndrome, Melnick-Needles Osteodysplasty, Melnick-Needles Syndrome, Membranous Lipodystrophy, Mendes Da Costa Syndrome, Meniere Disease, Ménière's Disease,

Meningeal Capillary Angiomatosis, Menkes Disease, Menke's Syndrome I, Mental Retardation Aphasia Shuffling Gait Adducted Thumbs (MASA), Mental Retardation-Deafness-Skeletal Abnormalities-Coarse Face with Full Lips, Mental Retardation with Hypoplastic 5th Fingernails and Toenails, Mental Retardation with Osteocartilaginous Abnormalities, Mental Retradation-X-linked with Growth Delay-Deafness-Microgenitalism, Menzel Type OPCA, Mermaid Syndrome, MERRF Syndrome, MERRF, Merten-Singleton Syndrome, MES, Mesangial IGA Nephropathy, Mesenteric Lipodystrophy, Mesiodens-Cataract Syndrome, Mesodermal Dysmorphodystrophy, Mesomelic Dwarfism-Madelung Deformity, Metabolic Acidosis, Metachromatic Leukodystrophy, Metatarsus Varus, Metatropic Dwarfism Syndrome, Metatropic Dysplasia, Metatropic Dysplasia I, Metatropic Dysplasia II, Methylmalonic Acidemia, Methylmalonic Aciduria, Meulengracht's Disease, MFD1, MG, MH, MHA, Micrencephaly, Microcephalic Primordial Dwarfism I, Microcephaly, Microcephaly-Hiatal Hernia-Nephrosis Galloway Type, Microcephaly-Hiatal Hernia-Nephrotic Syndrome, Microcystic Corneal Dystrophy, Microcythemia, Microlissencephaly, Microphthalmia, Microphthalmia or Anophthalmos with Associated Anomalies, Micropolygyria With Muscular Dystrophy, Microtia Absent Patellae Micrognathia Syndrome, Microvillus Inclusion Disease, MID, Midsystolic-click-late systolic murmur syndrome, Miescher's Type I Syndrome, Mikulicz Syndrome, Mikulicz-Radecki Syndrome, Mikulicz-Sjogren Syndrome, Mild Autosomal Recessive, Mild Intermediate Maple Syrup Urine Disease, Mild Maple Syrup Urine Disease, Miller Syndrome, Miller-Dieker Syndrome, Miller-Fisher Syndrome, Milroy Disease, Minkowski-Chauffard Syndrome, Minor Epilepsy, Minot-Von Willebrand Disease, Mirror-Image Dextrocardia, Mitochondrial Beta-Oxidation Disorders, Mitrochondrial and Cytosolic, Mitochondrial Cytopathy, Kearn-Sayre Type, Mitochondrial Encephalopathy, Mitochondrial Encephalomyopathy Lactic Acidosis and Strokelike Episodes, Mitochondrial Myopathy, Mitochondrial Myopathy Encephalopathy Lactic Acidosis Stroke-Like Episode, Mitochondrial PEPCK Deficiency, Mitral-valve prolapse, Mixed Apnea, Mixed Connective Tissue Disease, Mixed Hepatic Porphyria, Mixed Non-Fluent Aphasia, Mixed Sleep Apnea, Mixed Tonic and Clonic Torticollis, MJD, MKS, ML I, ML II, ML II, ML III, ML IV, ML Disorder Type I, ML Disorder Type II, ML Disorder Type III, ML Disorder Type IV, MLNS, MMR Syndrome,

MND, MNGIE, MNS, Mobitz I, Mobitz II, Mobius Syndrome, Moebius Syndrome, Moersch-Woltmann Syndrome, Mohr Syndrome, Monilethrix, Monomodal Visual Amnesia, Mononeuritis Multiplex, Mononeuritis Peripheral, Mononeuropathy Peripheral, Monosomy 3p2, Monosomy 9p Partial, Monosomy 11q Partial, Monosomy 13q Partial, Monosomy 18q Syndrome, Monosomy X, Monostotic Fibrous Dysplasia, Morgagni-Turner-Albright Syndrome, Morphea, Morquio Disease, Morquio Syndrome, Morquio Syndrome A, Morquio Syndrome B, Morquio-Brailsford Syndrome, Morvan Disease, Mosaic Tetrasomy 9p, Motor Neuron Disease, Motor Neuron Syndrome, Motor Neurone Disease, Motoneuron Disease, Motoneurone Disease, Motor System Disease (Focal and Slow), Moya-moya Disease, Moyamoya Disease, MPS, MPS I, MPS I H, MPS 1 H/S Hurler/Scheie Syndrome, MPS I S Scheie Syndrome, MPS II, MPS IIA, MPS IIB, MPS II-AR Autosomal Recessive Hunter Syndrome, MPS II-XR, MPS II-XR Severe Autosomal Recessive, MPS III, MPS III A B C and D Sanfiloppo A, MPS IV, MPS IV A and B Morquio A, MPS V, MPS VI, MPS VI Severe Intermediate Mild Maroteaux-Lamy, MPS VII, MPS VII Sly Syndrome, MPS VIII, MPS Disorder, MPS Disorder I, MPS Disorder II, MPS Disorder III, MPS Disorder VI, MPS Disorder Type VII, MRS, MS, MSA, MSD, MSL, MSS, MSUD, MSUD Type Ib, MSUD Type II, Mucocutaneous Lymph Node Syndrome, Mucolipidosis I, Mucolipidosis II, Mucolipidosis III, Mucolipidosis IV, Mucopolysaccharidosis, Mucopolysaccharidosis I-H, Mucopolysaccharidosis I-S, Mucopolysaccharidosis II, Mucopolysaccharidosis III, Mucopolysaccharidosis IV, Mucopolysaccharidosis VI, Mucopolysaccharidosis VII, Mucopolysaccharidosis Type I, Mucopolysaccharidosis Type II, Mucopolysaccharidosis Type III, Mucopolysaccharidosis Type VII, Mucosis, Mucosulfatidosis, Mucous Colitis, Mucoviscidosis, Mulibrey Dwarfism, Mulibrey Nanism Syndrome, Mullerian Duct Aplasia-Renal Aplasia-Cervicothoracic Somite Dysplasia, Mullerian Duct-Renal-Cervicothoracic-Upper Limb Defects, Mullerian Duct and Renal Agenesis with Upper Limb and Rib Anomalies, Mullerian-Renal-Cervicothoracic Somite Abnormalities, Multi-Infarct Dementia Binswanger's Type, Multicentric Castleman's Disease, Multifocal Eosinophilic Granuloma, Multiple Acyl-CoA Dehydrogenase Deficiency, Multiple Acyl-CoA Dehydrogenase Deficiency / Glutaric Aciduria Type II, Multiple Angiomas and Endochondromas, Multiple Carboxylase Deficiency, Multiple Cartilaginous Enchondroses,

Multiple Cartilaginous Exostoses, Multiple Enchondromatosis, Multiple Endocrine Deficiency Syndrome Type II, Multiple Epiphyseal Dysplasia, Multiple Exostoses, Multiple Exostoses Syndrome, Multiple Familial Polyposis, Multiple Lentigines Syndrome, Multiple Myeloma, Multiple Neuritis of the Shoulder Girdle, Multiple Osteochondromatosis, Multiple Peripheral Neuritis, Multiple Polyposis of the Colon, Multiple Pterygium Syndrome, Multiple Sclerosis, Multiple Sulfatase Deficiency, Multiple Symmetric Lipomatosis, Multiple System Atrophy, Multisynostotic Osteodysgenesis, Multisynostotic Osteodysgenesis with Long Bone Fractures, Mulvihill-Smith Syndrome, MURCS Association, Murk Jansen Type Metaphyseal Chondrodysplasia, Muscle Carnitine Deficiency, Muscle Core Disease, Muscle Phosphofructokinase Deficiency, Muscular Central Core Disease, Muscular Dystrophy, Muscular Dystrophy Classic X-linked Recessive, Muscular Dystrophy Congenital With Central Nervous System Involvement, Muscular Dystrophy Congenital Progressive with Mental Retardation, Muscular Dystrophy Facioscapulohumeral, Muscular Rheumatism, Muscular Rigidity - Progressive Spasm, Musculoskeletal Pain Syndrome, Mutilating Acropathy, Mutism, mvp, MVP, MWS, Myasthenia Gravis, Myasthenia Gravis Pseudoparalytica, Myasthenic Syndrome of Lambert-Eaton, Myelinoclastic Diffuse Sclerosis, Myelomatosis, Myhre Syndrome, Myoclonic Astatic Petit Mal Epilepsy, Myoclonic Dystonia, Myoclonic Encephalopathy of Infants, Myoclonic Epilepsy, Myoclonic Epilepsy Hartung Type, Myoclonus Epilepsy Associated with Ragged Red Fibers, Myoclonic Epilepsy and Ragged-Red Fiber Disease, Myoclonic Progressive Familial Epilepsy, Myoclonic Progressice Familial Epilepsy, Myoclonic Seizure, Myoclonus, Myoclonus Epilepsy, Myoencephalopathy Ragged-Red Fiber Disease, Myofibromatosis, Myofibromatosis Congenital, Myogenic Facio-Scapulo-Peroneal Syndrome, Myoneurogastointestinal Disorder and Encephalopathy, Myopathic Arthrogryposis Multiplex Congenita, Myopathic Carnitine Deficiency, Myopathy Central Fibrillar, Myopathy Congenital Nonprogressive, Myopathy Congenital Nonprogressive with Central Axis, Myopathy with Deficiency of Carnitine Palmitoyltransferase, Myopathy-Marinesco-Sjogren Syndrome, Myopathy-Metabolic Carnitine Palmitoyltransderase Deficiency, Myopathy Mitochondrial-Encephalopathy-Lactic Acidosis-Stroke, Myopathy with Sarcoplasmic Bodies and Intermediate Filaments, Myophosphorylase Deficiency, Myositis Ossificans Progressiv,

Myotonia Atrophica, Myotonia Congenita, Myotonia Congenita Intermittens, Myotonic Dystrophy, Myotonic Myopathy Dwarfism Chondrodystrophy Ocular and Facial Anomalies, Myotubular Myopathy, Myotubular Myopathy X-linked, Myproic Acid, Myriachit (Observed in Siberia), Myxedema, N-Acetylglucosamine-1-Phosphotransferase Deficiency, N-Acetyl Glutamate Synthetase Deficiency, NADH-CoQ reductase deficiency, Naegeli Ectodermal Dysplasias, Nager Syndrome, Nager Acrofacial Dysostosis Syndrome, Nager Syndrome, NAGS Deficiency, Nail Dystrophy-Deafness Syndrome, Nail Dysgenesis and Hypodontia, Nail-Patella Syndrome, Nance-Horan Syndrome, Nanocephalic Dwarfism, Nanocephaly, Nanophthalmia, Narcolepsy, Narcoleptic syndrome, NARP, Nasal-fronto-faciodysplasia, Nasal Alar Hypoplasia Hypothyroidism Pancreatic Achylia Congenital Deafness, Nasomaxillary Hypoplasia, Nasu Lipodystrophy, NBIA1, ND, NDI, NDP, Necrotizing Encephalomyelopathy of Leigh's, Necrotizing Respiratory Granulomatosis, Neill-Dingwall Syndrome, Nelson Syndrome, Nemaline Myopathy, Neonatal Adrenoleukodystrophy, Neonatal Adrenoleukodystrophy (NALD), Neonatal Adrenoleukodystrophy (ALD), Neonatal Autosomal Recessive Polycystic Kidney Disease, Neonatal Dwarfism, Neonatal Hepatitis, Neonatal Hypoglycemia, Neonatal Lactose Intolerance, Neonatal Lymphedema due to Exudative Enteropathy, Neonatal Progeroid Syndrome, Neonatal Pseudo-Hydrocephalic Progeroid Syndrome of Wiedemann-Rautenstrauch, Neoplastic Arachnoiditis, Nephroblastom, Nephrogenic Diabetes Insipidus, Nephronophthesis Familial Juvenile, Nephronophthesis Familial Juvenile, Nephropathic Cystinosis, Nephropathy-Pseudohermaphroditism-Wilms Tumor, Nephrosis-Microcephaly Syndrome, Nephrosis-Neuronal Dysmigration Syndrome, Nephrotic-Glycosuric-Dwarfism-Rickets-Hypophosphatemic Syndrome, Netherton Disease, Netherton Syndrome, Netherton Syndrome Ichthyosis, Nettleship Falls Syndrome (X-Linked), Neu-Laxova Syndrome, Neuhauser Syndrome, Neural-tube defects, Neuralgic Amyotrophy, Neuralgic Amyotrophy, Neuraminidase Deficiency, Neuraocutaneous melanosis, Neurinoma of the Acoustic Nerve, Neurinoma, Neuroacanthocytosis, Neuroaxonal Dystrophy Schindler Type, Neurodegeneration with brain iron accumulation type 1 (NBIA1), Neurofibroma of the Acoustic Nerve, Neurogenic Arthrogryposis Multiplex Congenita, Neuromyelitis Optica, Neuromyotonia, Neuromyotonia, Focal, Neuromyotonia, Generalized, Familial, Neuromytonia, Generalized,Sporadic, Neuronal

Axonal Dystrophy Schindler Type, Neuronal Ceroid Lipofuscinosis Adult Type, Neuronal Ceroid Lipofuscinosis Juvenile Type, Neuronal Ceroid Lipofuscinosis Type 1, Neuronopathic Acute Gaucher Disease, Neuropathic Amyloidosis, Neuropathic Beriberi, Neuropathy Ataxia and Retinitis Pigmentosa, Neuropathy of Brachialpelxus Syndrome, Neuropathy Hereditary Sensory Type I, Neuropathy Hereditary Sensory Type II, Neutral Lipid Storage Disease, Nevii, Nevoid Basal Cell Carcinoma Syndrome, Nevus, Nevus Cavernosus, Nevus Comedonicus, Nevus Depigmentosus, Nevus Sebaceous of Jadassohn, Nezelof's Syndrome, Nezelof's Thymic Aplasia, Nezelof Type Severe Combined Immunodeficiency, NF, NF1, NF2, NF-1, NF-2, NHS, Niemann Pick Disease, Nieman Pick disease Type A (acute neuronopathic form), Nieman Pick disease Type B, Nieman Pick Disease Type C (chronic neuronopathic form), Nieman Pick disease Type D (Nova Scotia variant), Nieman Pick disease Type E, Nieman Pick disease Type F (sea-blue histiocyte disease), Night Blindness, Nigrospinodentatal Degeneration, Niikawakuroki Syndrome, NLS, NM, Noack Syndrome Type I, Nocturnal Myoclonus Hereditary Essential Myoclonus, Nodular Cornea Degeneration, Non-Bullous CIE, Non-Bullous Congenital Ichthyosiform Erythroderma, Non-Communicating Hydrocephalus, Non-Deletion Type Alpha-Thalassemia / Mental Retardation syndrome, Non-Ketonic Hyperglycinemia Type I (NKHI), Non-Ketotic Hyperglycinemia, Non-Lipid Reticuloendotheliosis, Non-Neuronopathic Chronic Adult Gaucher Disease, Non-Scarring Epidermolysis Bullosa, Nonarteriosclerotic Cerebral Calcifications, Nonarticular Rheumatism, Noncerebral, Juvenile Gaucher Disease, Nondiabetic Glycosuria, Nonischemic Cardiomyopathy, Nonketotic Hypoglycemia and Carnitine Deficiency due to MCAD Deficiency, Nonketotic Hypoglycemia Caused by Deficiency of Acyl-CoA Dehydrogenase, Nonketotic Glycinemia, Nonne's Syndrome, Nonne-Milroy-Meige Syndrome, Nonopalescent Opalescent Dentine, Nonpuerperal Galactorrhea-Amenorrhea, Nonsecretory Myeloma, Nonspherocytic Hemolytic Anemia, Nontropical Sprue, Noonan Syndrome, Norepinephrine, Normal Pressure Hydrocephalus, Norman-Roberts Syndrome, Norrbottnian Gaucher Disease, Norrie Disease, Norwegian Type Hereditary Cholestasis, NPD, NPS, NS, NSA, Nuchal Dystonia Dementia Syndrome, Nutritional Neuropathy, Nyhan Syndrome, OAV Spectrum, Obstructive Apnea, Obstructive Hydrocephalus, Obstructive Sleep Apnea, OCC Syndrome, Occlusive Thromboaortopathy, OCCS, Occult

Intracranial Vascular Malformations, Occult Spinal Dysraphism Sequence, Ochoa Syndrome, Ochronosis, Ochronotic Arthritis, OCR, OCRL, Octocephaly, Ocular Albinism, Ocular Herpes, Ocular Myasthenia Gravis, Oculo-Auriculo-Vertebral Dysplasia, Oculo-Auriculo-Vertebral Spectrum, Oculo-Bucco-Genital Syndrome, Oculocerebral Syndrome with Hypopigmentation, Oculocerebrocutaneous Syndrome, Oculo-Cerebro-Renal, Oculocerebrorenal Dystrophy, Oculocerebrorenal Syndrome, Oculocraniosomatic Syndrome (obsolete), Oculocutaneous Albinism, Oculocutaneous Albinism Chediak-Higashi Type, Oculo-Dento-Digital Dysplasia, Oculodentodigital Syndrome, Oculo-Dento-Osseous Dysplasia, Oculo Gastrointestinal Muscular Dystrophy, Oculogastrointestinal Muscular Dystrophy, Oculomandibulodyscephaly with hypotrichosis, Oculomandibulofacial Syndrome, Oculomotor with Congenital Contractures and Muscle Atrophy, Oculosympathetic Palsy, ODD Syndrome, ODOD, Odontogenic Tumor, Odontotrichomelic Syndrome, OFD, OFD Syndrome, Ohio Type Amyloidosis (Type VII), OI, OI Congenita, OI Tarda, Oldfield Syndrome, Oligohydramnios Sequence, Oligophrenia Microphthalmos, Oligophrenic Polydystrophy, Olivopontocerebellar Atrophy, Olivopontocerebellar Atrophy with Dementia and Extrapyramidal Signs, Olivopontocerebellar Atrophy with Retinal Degeneration, Olivopontocerebellar Atrophy I, Olivopontocerebellar Atrophy II, Olivopontocerebellar Atrophy III, Olivopontocerebellar Atrophy IV, Olivopontocerebellar Atrophy V, Ollier Disease, Ollier Osteochondromatosis, Omphalocele-Visceromegaly-Macroglossia Syndrome, Ondine's Curse, Onion-Bulb Neuropathy, Onion Bulb Polyneuropathy, Onychoosteodysplasia, Onychotrichodysplasia with Neutropenia, OPCA, OPCA I, OPCA II, OPCA III, OPCA IV, OPCA V, OPD Syndrome, OPD Syndrome Type I, OPD Syndrome Type II, OPD I Syndrome, OPD II Syndrome, Ophthalmoarthropathy, Ophthalmoplegia-Intestinal Pseudoobstruction, Ophthalmoplegia, Pigmentary Degeneration of the Retina and Cadiomyopathy, Ophthalmoplegia Plus Syndrome, Ophthalmoplegia Syndrome, Opitz BBB Syndrome, Opitz BBB/G Compound Syndrome, Opitz BBBG Syndrome, Opitz-Frias Syndrome, Opitz G Syndrome, Opitz G/BBB Syndrome, Opitz Hypertelorism-Hypospadias Syndrome, Opitz-Kaveggia Syndrome, Opitz Oculogenitolaryngeal Syndrome, Opitz Trigonocephaly Syndrome, Opitz Syndrome, Opsoclonus, Opsoclonus-Myoclonus, Opthalmoneuromyelitis, Optic Atrophy Polyneuropathy and Deafness, Optic

Neuroencephalomyelopathy, Optic Neuromyelitis, Opticomyelitis, Optochiasmatic Arachnoiditis, Oral-Facial Clefts, Oral-facial Dyskinesia, Oral Facial Dystonia, Oral-Facial-Digital Syndrome, Oral-Facial-Digital Syndrome Type I, Oral-Facial-Digital Syndrome I, Oral-Facial-Digital Syndrome II, Oral-Facial-Digital Syndrome III, Oral-Facial-Digital Syndrome IV, Orbital Cyst with Cerebral and Focal Dermal Malformations, Ornithine Carbamyl Transferase Deficiency, Ornithine Transcarbamylase Deficiency, Orocraniodigital Syndrome, Orofaciodigital Syndrome, Oromandibular Dystonia, Orthostatic Hypotension, Osler-Weber-Rendu disease, Osseous-Oculo-Dento Dysplasia, Osteitis deformans, Osteochondrodystrophy Deformans, Osteochondroplasia, Osteodysplasty of Melnick and Needles, Osteogenesis Imperfect, Osteogenesis Imperfecta, Osteogenesis Imperfecta Congenita, Osteogenesis Imperfecta Tarda, Osteohypertrophic Nevus Flammeus, Osteopathia Hyperostotica Scleroticans Multiplex Infantalis, Osteopathyrosis, Osteopetrosis, Osteopetrosis Autosomal Dominant Adult Type, Osteopetrosis Autosomal Recessive Malignant Infantile Type, Osteopetrosis Mild Autosomal Recessive Intermediate Typ, Osteosclerosis Fragilis Generalisata, Osteosclerotic Myeloma, Ostium Primum Defect (endocardial cushion defects included), Ostium Secundum Defect, OTC Deficiency, Oto Palato Digital Syndrome, Oto-Palato-Digital Syndrome Type I, Oto-Palatal-Digital Syndrome Type II, Otodental Dysplasia, Otopalatodigital Syndrome, Otopalataldigital Syndrome Type II, Oudtshoorn Skin, Ovarian Dwarfism Turner Type, Ovary Aplasia Turner Type, OWR, Oxalosis, Oxidase deficiency, Oxycephaly, Oxycephaly-Acrocephaly, P-V, PA, PAC, Pachyonychia Ichtyosiforme, Pachyonychia Congenita with Natal Teeth, Pachyonychia Congenita, Pachyonychia Congenita Keratosis Disseminata Circumscripta (follicularis), Pachyonychia Congenita Jadassohn-Lewandowsky Type, PAF with MSA, Paget's Disease, Paget's Disease of Bone, Paget's Disease of the Breast, Paget's Disease of the Nipple, Paget's Disease of the Nipple and Areola, Pagon Syndrome, Painful Ophthalmoplegia, PAIS, Palatal Myoclonus, Palato-Oto-Digital Syndrome, Palatal-Oto-Digital Syndrome Type I, Palatal-Oto-Digital Syndrome Type II, Pallister Syndrome, Pallister-Hall Syndrome, Pallister-Killian Mosaic Syndrome, Pallister Mosaic Aneuploidy, Pallister Mosaic Syndrome, Pallister Mosaic Syndrome Tetrasomy 12p, Pallister-W Syndrome, Palmoplantar Hyperkeratosis and Alopecia, Palsy, Pancreatic Fibrosis, Pancreatic

Insufficiency and Bone Marrow Dysfunction, Pancreatic Ulcerogenic Tumor Syndrome, Panmyelophthisis, Panmyelopathy, Pantothenate kinase associated neurodegeneration (PKAN), Papillon-Lefevre Syndrome, Papillotonic Psuedotabes, Paralysis Periodica Paramyotonica, Paralytic Beriberi, Paralytic Brachial Neuritis, Paramedian Lower Lip Pits-Popliteal Pyerygium Syndrome, Paramedian Diencephalic Syndrome, Paramyeloidosis, Paramyoclonus Multiple, Paramyotonia Congenita, Paramyotonia Congenita of Von Eulenburg, Parkinson's disease, Paroxysmal Atrial Tachycardia, Paroxysmal Cold Hemoglobinuria, Paroxysmal Dystonia, Paroxysmal Dystonia Choreathetosis, Paroxysmal Kinesigenic Dystonia, Paroxysmal Nocturnal Hemoglobinuria, Paroxysmal Normal Hemoglobinuria, Paroxysmal Sleep, Parrot Syndrome, Parry Disease, Parry-Romberg Syndrome, Parsonage-Turner Syndrome, Partial Androgen Insensitivity Syndrome, Partial Deletion of the Short Arm of Chromosome 4, Partial Deletion of the Short Arm of Chromosome 5, Partial Deletion of Short Arm of Chromosome 9, Partial Duplication 3q Syndrome, Partial Duplication 15q Syndrome, Partial Facial Palsy With Urinary Abnormalities, Partial Gigantism of Hands and Feet- Nevi-Hemihypertrophy-Macrocephaly, Partial Lipodystrophy, Partial Monosomy of Long Arm of Chromosome 11, Partial Monosomy of the Long Arm of Chromosome 13, Partial Spinal Sensory Syndrome, Partial Trisomy 11q, Partington Syndrome, PAT, Patent Ductus Arteriosus, Pathological Myoclonus, Pauciarticular-Onset Juvenile Arthritis, Pauciarticular-Onset Juvenile Arthritis, Paulitis, PBC, PBS, PC Deficiency, PC Deficiency Group A, PC Deficiency Group B, PC, Eulenburg Disease, PCC Deficiency, PCH, PCLD, PCT, PD, PDA, PDH Deficiency, Pearson Syndrome Pyruvate Carboxylase Deficiency, Pediatric Obstructive Sleep Apnea, Peeling Skin Syndrome, Pelizaeus-Merzbacher Disease, Pelizaeus-Merzbacher Brain Sclerosis, Pelizaeus-Merzbacher Brain Sclerosis, Pellagra-Cerebellar Ataxia-Renal Aminoaciduria Syndrome, Pelvic Pain Syndrome, Pemphigus Vulgaris, Pena Shokeir II Syndrome, Pena Shokeir Syndrome Type II, Penile Fibromatosis, Penile Fibrosis, Penile Induration, Penta X Syndrome, Pentalogy of Cantrell, Pentalogy Syndrome, Pentasomy X, PEPCK Deficiency, Pepper Syndrome, Perheentupa Syndrome, Periarticular Fibrositis, Pericardial Constriction with Growth Failure, Pericollagen Amyloidosis, Perinatal Polycystic Kidney Diseases, Perineal Anus, Periodic Amyloid Syndrome, Periodic Peritonitis Syndrome, Periodic Somnolence and Morbid

Hunger, Periodic Syndrome, Peripheral Cystoid Degeneration of the Retina, Peripheral Dysostosis-Nasal Hypoplasia-Mental Retardation, Peripheral Neuritis, Peripheral Neuropathy, Peritoneopericardial Diaphragmatic Hernia, Pernicious Anemia, Peromelia with Micrognathia, Peroneal Muscular Atrophy, Peroneal Nerve Palsy, Peroutka Sneeze, Peroxisomal Acyl-CoA Oxidase, Peroxisomal Beta-Oxidation Disorders, Peroxisomal Bifunctional Enzyme, Peroxisomal Thiolase, Peroxisomal Thiolase Deficiency, Persistent Truncus Arteriosus, Perthes Disease, Petit Mal Epilepsy, Petit Mal Variant, Peutz-Jeghers Syndrome, Peutz-Touraine Syndrome, Peyronie Disease, Pfeiffer, Pfeiffer Syndrome Type I, PGA I, PGA II,PGA III, PGK, PH Type I, Pharyngeal Pouch Syndrome, PHD Short-Chain Acyl-CoA Dehydrogenase Deficiency, Phenylalanine Hydroxylase Deficiency, Phenylalaninemia, Phenylketonuria, Phenylpyruvic Oligophrenia, Phocomelia, Phocomelia Syndrome, Phosphoenolpyruvate Carboxykinase Deficiency, Phosphofructokinase Deficiency, Phosphoglycerate Kinase Deficiency, Phosphoglycerokinase, Phosphorylase 6 Kinase Deficiency, Phosphorylase Deficiency Glycogen Storage Disease, Phosphorylase Kinase Deficiency of Liver, Photic Sneeze Reflex, Photic Sneezing, Phototherapeutic keratectomy, PHS, Physicist John Dalton, Phytanic Acid Storage Disease, Pi Phenotype ZZ, PI, Pick Disease of the Brain, Pick's Disease, Pickwickian Syndrome, Pierre Robin Anomalad, Pierre Robin Complex, Pierre Robin Sequence, Pierre Robin Syndrome, Pierre Robin Syndrome with Hyperphalangy and Clinodactyly, Pierre-Marie's Disease, Pigmentary Degeneration of Globus Pallidus Substantia Nigra Red Nucleus, Pili Torti and Nerve Deafness, Pili Torti-Sensorineural Hearing Loss, Pituitary Dwarfism II, Pituitary Tumor after Adrenalectomy, Pityriasis Pilaris, Pityriasis Rubra Pilaris, PJS, PKAN, PKD, PKD1, PKD2, PKD3, PKU, PKU1, Plagiocephaly, Plasma Cell Myeloma, Plasma Cell Leukemia, Plasma Thromboplastin Component Deficiency, Plasma Transglutaminase Deficiency, Plastic Induration Corpora Cavernosa, Plastic Induration of the Penis, PLD, Plicated Tongue, PLS, PMD, Pneumorenal Syndrome, PNH, PNM, PNP Deficiency, POD, POH, Poikiloderma Atrophicans and Cataract, Poikiloderma Congenitale, Poland Anomaly, Poland Sequence, Poland Syndactyly, Poland Syndrome, Poliodystrophia Cerebri Progressiva, Polyarthritis Enterica, Polyarteritis Nodosa, Polyarticular-Onset Juvenile Arthritis Type I, Polyarticular-Onset Juvenile Arthritis Type II, Polyarticular-Onset Juvenile Arthritis Types I and II, Polychondritis, Polycystic Kidney Disease,

Polycystic Kidney Disease Medullary Type, Polycystic Liver Disease, Polycystic Ovary Disease, Polycystic Renal Diseases, Polydactyly-Joubert Syndrome, Polydysplastic Epidermolysis Bullosa, Polydystrophia Oligophrenia, Polydystrophic Dwarfism, Polyglandular Autoimmune Syndrome Type III, Polyglandular Autoimmune Syndrome Type II, Polyglandular Autoimmune Syndrome Type I, Polyglandular Deficiency Syndrome Type II, Polyglandular Syndromes, Polymorphic Macula Lutea Degeneration, Polymorphic Macular Degeneration, Polymorphism of Platelet Glycoprotien Ib, Polymorphous Corneal Dystrophy Hereditary, Polymyalgia Rheumatica, Polymyositis and Dermatomyositis, Primary Agammaglobulinemia, Polyneuritis Peripheral, Polyneuropathy-Deafness-Optic Atrophy, Polyneuropathy Peripheral, Polyneuropathy and Polyradiculoneuropathy, Polyostotic Fibrous Dysplasia, Polyostotic Sclerosing Histiocytosis, Polyposis Familial, Polyposis Gardner Type, Polyposis Hamartomatous Intestinal, Polyposis-Osteomatosis-Epidermoid Cyst Syndrome, Polyposis Skin Pigmentation Alopecia and Fingernail Changes, Polyps and Spots Syndrome, Polyserositis Recurrent, Polysomy Y, Polysyndactyly with Peculiar Skull Shape, Polysyndactyly-Dysmorphic Craniofacies Greig Type, Pompe Disease, Popliteal Pterygium Syndrome, Porcupine Man, Porencephaly, Porphobilinogen deaminase (PBG-D), Porphyria, Porphyria Acute Intermittent, Porphyria ALA-D, Porphyria Cutanea Tarda, Porphyria Cutanea Tarda Hereditaria, Porphyria Cutanea Tarda Symptomatica, Porphyria Hepatica Variegate, Porphyria Swedish Type, Porphyria Variegate, Porphyriam Acute Intermittent, Porphyrins, Porrigo Decalvans, Port Wine Stains, Portuguese Type Amyloidosis, Post-Infective Polyneuritis, Postanoxic Intention Myoclonus, Postaxial Acrofacial Dysostosis, Postaxial Polydactyly, Postencephalitic Intention Myoclonus, Posterior Corneal Dystrophy Hereditary, Posterior Thalamic Syndrome, Postmyelographic Arachnoiditis, Postnatal Cerebral Palsy, Postoperative Cholestasis, Postpartum Galactorrhea-Amenorrhea Syndrome, Postpartum Hypopituitarism, Postpartum Panhypopituitary Syndrome, Postpartum Panhypopituitarism, Postpartum Pituitary Necrosis, Postural Hypotension, Potassium-Losing Nephritis, Potassium Loss Syndrome, Potter Type I Infantile Polycystic Kidney Diseases, Potter Type III Polycystic Kidney Disease, PPH, PPS, Prader-Willi Syndrome, Prader-Labhart-Willi Fancone Syndrome, Prealbumin Tyr-77 Amyloidosis, Preexcitation Syndrome, Pregnenolone Deficiency, Premature Atrial Contractions,

Premature Senility Syndrome, Premature Supraventricular Contractions, Premature Ventricular Complexes, Prenatal or Connatal Neuroaxonal Dystrophy, Presenile Dementia, Presenile Macula Lutea Retinae Degeneration, Primary Adrenal Insufficiency, Primary Agammaglobulinemias, Primary Aldosteronism, Primary Alveolar Hypoventilation, Primary Amyloidosis, Primary Anemia, Primary Anemia, Primary Beriberi, Primary Biliary, Primary Biliary Cirrhosis, Primary Brown Syndrome, Primary Carnitine Deficiency, Primary Central Hypoventilation Syndrome, Primary Ciliary Dyskinesia Kartagener Type, Primary Cutaneous Amyloidosis, Primary Dystonia, Primary Failure Adrenocortical Insufficiency, Primary Familial Hypoplasia of the Maxilla, Primary Hemochromatosis, Primary Hyperhidrosis, Primary Hyperoxaluria Type 1 (PH1), Primary Hyperoxaluria Type 1, Primary Hyperoxaluria Type II, Primary Hyperoxaluria Type III, Primary Hypogonadism, Primary Intestinal Lymphangiectasia, Primary Lateral Sclerosis, Primary Nonhereditary Amyloidosis, Primary Obliterative Pulmonary Vascular Disease, Primary Progressive Multiple Sclerosis, Primary Pulmonary Hypertension, Primary Reading Disability, Primary Renal Glycosuria, Primary Sclerosing Cholangitis, Primary Thrombocythemia, Primary Tumors of Central Nervous System, Primary Visual Agnosia, Proctocolitis Idiopathic, Progeria of Adulthood, Progeria of Childhood, Progeroid Nanism, Progeriod Short Stature with Pigmented Nevi, Progeroid Syndrome of De Barsy, Progressive Autonomic Failure with Multiple System Atrophy, Progressive Bulbar Palsy, Progressive Bulbar Palsy Included, Progressive Cardiomyopathic Lentiginosis, Progressive Cerebellar Ataxia Familial, Progressive Cerebral Poliodystrophy, Progressive Choroidal Atrophy, Progressive Diaphyseal Dysplasia, Progressive Facial Hemiatrophy, Progressive Familial Myoclonic Epilepsy, Progressive Hemifacial Atrophy, Progressive Hypoerythemia, Progressive Infantile Poliodystrophy, Progressive Lenticular Degeneration, Progressive Lipodystrophy, Progressive Muscular Dystrophy of Childhood, Progressive Myoclonic Epilepsy, Progressive Osseous Heteroplasia, Progressive Pallid Degeneration Syndrome, Progressive Spinobulbar Muscular Atrophy, Progressive Supranuclear Palsy, Progressive Systemic Sclerosis, Progressive Tapetochoroidal Dystrophy, Proline Oxidase Deficiency, Propionic Acidemia, Propionic Acidemia Type I (PCCA Deficiency), Propionic Acidemia Type II (PCCB Deficiency), Propionyl CoA Carboxylase Deficiency, Protanomaly, Protanopia, Protein-Losing Enteropathy Secondary

to Congestive Heart Failure, Proteus Syndrome, Proximal Deletion of 4q-Included, PRP, PRS, Prune Belly Syndrome, PS, Pseudo-Hurler Polydystrophy, Pseudo-Polydystrophy, Pseudoacanthosis Nigricans, Pseudoachondroplasia, Pseudocholinesterase Deficiency, Pseudogout Familial, Pseudohemophilia, Pseudohermaphroditism, Pseudohermaphroditism-Nephron Disorder-Wilm's Tumor, Pseudohypertrophic Muscular Dystrophy, Pseudohypoparathyroidism, Pseudohypophosphatasia, Pseudopolydystrophy, Pseudothalidomide Syndrome, Pseudoxanthoma Elasticum, Psoriasis, Psorospermosis Follicularis, PSP, PSS, Psychomotor Convulsion, Psychomotor Epilepsy, Psychomotor Equivalent Epilepsy, PTC Deficiency, Pterygium, Pterygium Colli Syndrome, Pterygium Universale, Pterygolymphangiectasia, Pulmonary Atresia, Pulmonary Lymphangiomyomatosis, Pulmonary Stenosis, Pulmonic Stenosis-Ventricular Septal Defect, Pulp Stones, Pulpal Dysplasia, Pulseless Disease, Pure Alymphocytosis, Pure Cutaneous Histiocytosis, Purine Nucleoside Phosphorylase Deficiency, Purpura Hemorrhagica, Purtilo Syndrome, PXE, PXE Dominant Type, PXE Recessive Type, Pycnodysostosis, Pyknoepilepsy, Pyroglutamic Aciduria, Pyroglutamicaciduria, Pyrroline Carboxylate Dehydrogenase Deficiency, Pyruvate Carboxylase Deficiency, Pyruvate Carboxylase Deficiency Group A, Pyruvate Carboxylase Deficiency Group B, Pyruvate Dehydrogenase Deficiency, Pyruvate Kinase Deficiency, q25-qter, q26 or q27-qter, q31 or 32-qter, QT Prolongation with Extracellular Hypohypocalcinemia, QT Prolongation without Congenital Deafness, QT Prolonged with Congenital Deafness, Quadriparesis of Cerebral Palsy, Quadriplegia of Cerebral Palsy, Quantal Squander, r4, r6, r14, r 18, r21, r22, Rachischisis Posterior, Radial Aplasia-Amegakaryocytic Thrombocytopenia, Radial Aplasia-Thrombocytopenia Syndrome, Radial Nerve Palsy, Radicular Neuropathy Sensory, Radicular Neuropathy Sensory Recessive, Radicular Dentin Dysplasia, Rapid-onset Dystonia-parkinsonism, Rapp-Hodgkin Syndrome, Rapp-Hodgkin (hypohidrotic) Ectodermal Dysplasia syndrome, Rapp-Hodgkin Hypohidrotic Ectodermal Dysplasias, Rare hereditary ataxia with polyneuritic changes and deafness caused by a defect in the enzyme phytanic acid hydroxylase, Rautenstrauch-Wiedemann Syndrome, Rautenstrauch-Wiedemann Type Neonatal Progeria, Raynaud's Phenomenon, RDP, Reactive Functional Hypoglycemia, Reactive Hypoglycemia Secondary to Mild Diabetes, Recessive Type Kenny-Caffe Syndrome, Recklin Recessive Type Myotonia Congenita, Recklinghausen

Disease, Rectoperineal Fistula, Recurrent Vomiting, Reflex Neurovascular Dystrophy, Reflex Sympathetic Dystrophy Syndrome, Refractive Errors, Refractory Anemia, Refrigeration Palsy, Refsum Disease, Refsum's Disease, Regional Enteritis, Reid-Barlow's syndrome, Reifenstein Syndrome, Reiger Anomaly-Growth Retardation, Reiger Syndrome, Reimann Periodic Disease, Reimann's Syndrome, Reis-Bucklers Corneal Dystrophy, Reiter's Syndrome, Relapsing Guillain-Barre Syndrome, Relapsing-Remitting Multiple Sclerosis, Renal Agenesis, Renal Dysplasia-Blindness Hereditary, Renal Dysplasia-Retinal Aplasia Loken-Senior Type, Renal Glycosuria, Renal Glycosuria Type A, Renal Glycosuria Type B, Renal Glycosuria Type O, Renal-Oculocerebrodystrophy, Renal-Retinal Dysplasia with Medullary Cystic Disease, Renal-Retinal Dystrophy Familial, Renal-Retinal Syndrome, Rendu-Osler-Weber Syndrome, Respiratory Acidosis, Respiratory Chain Disorders, Respiratory Myoclonus, Restless Legs Syndrome, Restrictive Cardiomyopathy, Retention Hyperlipemia, Rethore Syndrome (obsolete), Reticular Dysgenesis, Retinal Aplastic-Cystic Kidneys-Joubert Syndrome, Retinal Cone Degeneration, Retinal Cone Dystrophy, Retinal Cone-Rod Dystrophy, Retinitis Pigmentosa, Retinitis Pigmentosa and Congenital Deafness, Retinoblastoma, Retinol Deficiency, Retinoschisis, Retinoschisis Juvenile, Retraction Syndrome, Retrobulbar Neuropathy, Retrolenticular Syndrome, Rett Syndrome, Reverse Coarction, Reye Syndrome, Reye's Syndrome, RGS, Rh Blood Factors, Rh Disease, Rh Factor Incompatibility, Rh Incompatibility, Rhesus Incompatibility, Rheumatic Fever, Rheumatoid Arthritis, Rheumatoid Myositis, Rhinosinusogenic Cerebral Arachnoiditis, Rhizomelic Chondrodysplasia Punctata (RCDP),Acatalasemia,Classical Refsum disease, RHS, Rhythmical Myoclonus, Rib Gap Defects with Micrognathia, Ribbing Disease (obsolete), Ribbing Disease, Richner-Hanhart Syndrome, Rieger Syndrome, Rieter's Syndrome, Right Ventricular Fibrosis, Riley-Day Syndrome, Riley-Smith syndrome, Ring Chromosome 14, Ring Chromosome 18, Ring 4, Ring 4 Chromosome, Ring 6, Ring 6 Chromosome, Ring 9, Ring 9 Chromosome R9, Ring 14, Ring 15, Ring 15 Chromosome (mosaic pattern), Ring 18, Ring Chromosome 18, Ring 21, Ring 21 Chromosome, Ring 22, Ring 22 Chromosome, Ritter Disease, Ritter-Lyell Syndrome, RLS, RMSS, Roberts SC-Phocomelia Syndrome, Roberts Syndrome, Roberts Tetraphocomelia Syndrome, Robertson's Ectodermal Dysplasias, Robin Anomalad, Robin Sequence, Robin Syndrome,

Robinow Dwarfism, Robinow Syndrome, Robinow Syndrome Dominant Form, Robinow Syndrome Recessive Form, Rod Myopathy, Roger Disease, Rokitansky's Disease, Romano-Ward Syndrome, Romberg Syndrome, Rootless Teeth, Rosenberg-Chutorian Syndrome, Rosewater Syndrome, Rosselli-Gulienatti Syndrome, Rothmund-Thomson Syndrome, Roussy-Levy Syndrome, RP, RS X-Linked, RS, RSDS, RSH Syndrome, RSS, RSTS, RTS, Rubella Congenital, Rubinstein Syndrome, Rubinstein-Taybi Syndrome, Rubinstein Taybi Broad Thumb-Hallux syndrome, Rufous Albinism, Ruhr's Syndrome, Russell's Diencephalic Cachexia, Russell's Syndrome, Russell Syndrome, Russell-Silver Dwarfism, Russell-Silver Syndrome, Russell-Silver Syndrome X-linked, Ruvalcaba-Myhre-Smith syndrome (RMSS), Ruvalcaba Syndrome, Ruvalcaba Type Osseous Dysplasia with Mental Retardation, Sacral Regression, Sacral Agenesis Congenital, SAE, Saethre-Chotzen Syndrome, Sakati, Sakati Syndrome, Sakati-Nyhan Syndrome, Salaam Spasms, Salivosudoriparous Syndrome, Salzman Nodular Corneal Dystrophy, Sandhoff Disease, Sanfilippo Syndrome, Sanfilippo Type A, Sanfilippo Type B, Santavuori Disease, Santavuori-Haltia Disease, Sarcoid of Boeck, Sarcoidosis, Sathre-chotzen, Saturday Night Palsy, SBMA, SC Phocomelia Syndrome, SC Syndrome, SCA 3, SCAD Deficiency, SCAD Deficiency Adult-Onset Localized, SCAD Deficiency Congenital Generalized, SCAD, SCADH Deficiency, Scalded Skin Syndrome, Scalp Defect Congenital, Scaphocephaly, Scaphocephaly, Scapula Elevata, Scapuloperoneal Myopathy, Scapuloperoneal Muscular Dystrophy, Scapuloperoneal Syndrome Myopathic Type, Scarring Bullosa, SCHAD, Schaumann's Disease, Scheie Syndrome, Schereshevkii-Turner Syndrome, Schilder Disease, Schilder Encephalitis, Schilder's Disease, Schindler Disease Type I (Infantile Onset), Schindler Disease Infantile Onset, Schindler Disease, Schindler Disease Type II (Adult Onset), Schinzel Syndrome, Schinzel-Giedion Syndrome, Schinzel Acrocallosal Syndrome, Schinzel-Giedion Midface-Retraction Syndrome, Schizencephaly, Schmid Type Metaphyseal Chondrodysplasia, Schmid Metaphyseal Dysostosis, Schmid-Fraccaro Syndrome, Schmidt Syndrome, Schopf-Schultz-Passarge Syndrome, Schueller-Christian Disease, Schut-Haymaker Type, Schwartz-Jampel-Aberfeld Syndrome, Schwartz-Jampel Syndrome Types 1A and 1B, Schwartz-Jampel Syndrome, Schwartz-Jampel Syndrome Type 2, SCID, Scleroderma, Sclerosis Familial Progressive Systemic, Sclerosis Diffuse Familial Brain, Scott Craniodigital Syndrome With Mental Retardation,

Scrotal Tongue, SCS, SD, SDS, SDYS, Seasonal Conjunctivitis, Sebaceous Nevus Syndrome, Sebaceous nevus, Seborrheic Keratosis, Seborrheic Warts, Seckel Syndrome, Seckel Type Dwarfism, Second Degree Congenital Heart Block, Secondary Amyloidosis, Secondary Blepharospasm, Secondary Non-tropical Sprue, Secondary Brown Syndrome, Secondary Beriberi, Secondary Generalized Amyloidosis, Secondary Dystonia, Secretory Component Deficiency, Secretory IgA Deficiency, SED Tarda, SED Congenital, SEDC, Segmental linear achromic nevus, Segmental Dystonia, Segmental Myoclonus, Seip Syndrome, Seitelberger Disease, Seizures, Selective Deficiency of IgG Subclasses, Selective Mutism, Selective Deficiency of IgG Subclass, Selective IgM Deficiency, Selective Mutism, Selective IgA Deficiency, Self-Healing Histiocytosis, Semilobar Holoprosencephaly, Seminiferous Tubule Dysgenesis, Senile Retinoschisis, Senile Warts, Senior-Loken Syndrome, Sensory Neuropathy Hereditary Type I, Sensory Neuropathy Hereditary Type II, Sensory Radicular Neuropathy, Sensory Radicular Neuropathy Recessive, Septic Progressive Granulomatosis, Septo-Optic Dysplasia, Serous Circumscribed Meningitis, Serum Protease Inhibitor Deficiency, Serum Carnosinase Deficiency, Setleis Syndrome, Severe Combined Immunodeficiency, Severe Combined Immunodeficiency with Adenosine Deaminase Deficiency, Severe Combined Immunodeficiency (SCID), Sex Reversal, Sexual Infantilism, SGB Syndrome, Sheehan Syndrome, Shields Type Dentinogenesis Imperfecta, Shingles,varicella-zoster virus, Ship Beriberi, SHORT Syndrome, Short Arm 18 Deletion Syndrome, Short Chain Acyl CoA Dehydrogenase Deficiency, Short Chain Acyl-CoA Dehydrogenase (SCAD) Deficiency, Short Stature and Facial Telangiectasis, Short Stature Facial/Skeletal Anomalies-Retardation-Macrodontia, Short Stature-Hyperextensibility-Rieger Anomaly-Teething Delay, Short Stature-Onychodysplasia, Short Stature Telangiectatic Erythema of the Face, SHORT Syndrome, Shoshin Beriberi, Shoulder girdle syndrome, Shprintzen-Goldberg Syndrome, Shulman Syndrome, Shwachman-Bodian Syndrome, Shwachman-Diamond Syndrome, Shwachman-Diamond-Oski Syndrome, Shwachmann Syndrome, Shy Drager Syndrome, Shy-Magee Syndrome, SI Deficiency, Sialidase Deficiency, Sialidosis Type I Juvenile, Sialidosis Type II Infantile, Sialidosis, Sialolipidosis, Sick Sinus Syndrome, Sickle Cell Anemia, Sickle Cell Disease, Sickle Cell-Hemoglobin C Disease, Sickle Cell-Hemoglobin D Disease, Sickle Cell-Thalassemia Disease, Sickle Cell Trait, Sideroblastic

Anemias, Sideroblastic Anemia, Sideroblastosis, SIDS, Siegel-Cattan-Mamou Syndrome, Siemens-Bloch type Pigmented Dermatosis, Siemens Syndrome, Siewerling-Creutzfeldt Disease, Siewert Syndrome, Silver Syndrome, Silver-Russell Dwarfism, Silver-Russell Syndrome, Simmond's Disease, Simons Syndrome, Simplex Epidermolysis Bullosa, Simpson Dysmorphia Syndrome, Simpson-Golabi-Behmel Syndrome, Sinding-Larsen-Johansson Disease, Singleton-Merten Syndrome, Sinus Arrhythmia, Sinus Venosus, Sinus tachycardia, Sirenomelia Sequence, Sirenomelus, Situs Inversus Bronchiectasis and Sinusitis, SJA Syndrome, Sjogren Larsson Syndrome Ichthyosis, Sjogren Syndrome, Sjogren Larsson Syndrome Ichthyosis, Sjögren's Syndrome, SJS, Skeletal dysplasia, Skeletal Dysplasia Weismann Netter Stuhl Type, Skin Peeling Syndrome, Skin Neoplasms, Skull Asymmetry and Mild Retardation, Skull Asymmetry and Mild Syndactyly, SLE, Sleep Epilepsy, Sleep Apnea, SLO, Sly Syndrome, SMA, SMA Infantile Acute Form, SMA I, SMA III, SMA type I, SMA type II, SMA type III, SMA3, SMAX1, SMCR, Smith Lemli Opitz Syndrome, Smith Magenis Syndrome, Smith-Magenis Chromosome Region, Smith-McCort Dwarfism, Smith-Opitz-Inborn Syndrome, Smith Disease, Smoldering Myeloma, SMS, SNE, Sneezing From Light Exposure, Sodium valproate, Solitary Plasmacytoma of Bone, Sorsby Disease, Sotos Syndrome, Souques-Charcot Syndrome, South African Genetic Porphyria, Spasmodic Dysphonia, Spasmodic Torticollis, Spasmodic Wryneck, Spastic Cerebral Palsy, Spastic Colon, Spastic Dysphonia, Spastic Paraplegia, SPD Calcinosis, Specific Antibody Deficiency with Normal Immunoglobulins, Specific Reading Disability, SPH2, Spherocytic Anemia, Spherocytosis, Spherophakia-Brachymorphia Syndrome, Sphingomyelin Lipidosis, Sphingomyelinase Deficiency, Spider fingers, Spielmeyer-Vogt Disease, Spielmeyer-Vogt-Batten Syndrome, Spina Bifida, Spina Bifida Aperta, Spinal Arachnoiditis, Spinal Arteriovenous Malformation, Spinal Ataxia Hereditofamilial, Spinal and Bulbar Muscular Atrophy, Spinal Diffuse Idiopathic Skeletal Hyperostosis, Spinal DISH, Spinal Muscular Atrophy, Spinal Muscular Atrophy All Types, Spinal Muscular Atrophy Type ALS, Spinal Muscular Atrophy-Hypertrophy of the Calves, Spinal Muscular Atrophy Type I, Spinal Muscular Atrophy Type III, Spinal Muscular Atrophy type 3, Spinal Muscular Atrophy-Hypertrophy of the Calves, Spinal Ossifying Arachnoiditis, Spinal Stenosis, Spino Cerebellar Ataxia, Spinocerebellar Atrophy Type I, Spinocerebellar Ataxia Type I (SCA1), Spinocerebellar

Ataxia Type II (SCAII), Spinocerebellar Ataxia Type III (SCAIII), Spinocerebellar Ataxia Type III (SCA 3), Spinocerebellar Ataxia Type IV (SCAIV), Spinocerebellar Ataxia Type V (SCAV), Spinocerebellar Ataxia Type VI (SCAVI), Spinocerebellar Ataxia Type VII (SCAVII), Spirochetal Jaundice, Splenic Agenesis Syndrome, Splenic Ptosis, Splenoptosis, Split Hand Deformity-Mandibulofacial Dysostosis, Split Hand Deformity-Mandibulofacial Dysostosis, Split-Hand Deformity, Spondyloarthritis, Spondylocostal Dysplasia - Type I, Spondyloepiphyseal Dysplasia Tarda, Spondylothoracic Dysplasia, Spondylotic Caudal Radiculopathy, Sponge Kidney, Spongioblastoma Multiforme, Spontaneous Hypoglycemia, Sprengel Deformity, Spring Ophthalmia, SRS, ST, Stale Fish Syndrome, Staphyloccal Scalded Skin Syndrome, Stargardt's Disease, Startle Disease, Status Epilepticus, Steele-Richardson-Olszewski Syndrome, Steely Hair Disease, Stein-Leventhal Syndrome, Steinert Disease, Stengel's Syndrome, Stengel-Batten-Mayou-Spielmeyer-Vogt-Stock Disease, Stenosing Cholangitis, Stenosis of the Lumbar Vertebral Canal, Stenosis, Steroid Sulfatase Deficiency, Stevanovic's Ectodermal Dysplasias, Stevens Johnson Syndrome, Stevens-Johnson Syndrome, STGD, Stickler Syndrome, Stiff-Man Syndrome, Stiff Man Syndrome, Stiff Person Syndrome, Still's Disease, Stilling-Turk-Duane Syndrome, Stillís Disease, Stimulus-Sensitive Myoclonus, Stone Man Syndrome, Stone Man, Streeter Anomaly, Striatonigral Degeneration Autosomal Dominant Type, Striopallidodentate Calcinosis, Stroma, Descemet's Membrane, Stromal Corneal Dystrophy, Struma Lymphomatosa, Sturge-Kalischer-Weber Syndrome, Sturge Weber Syndrome, Sturge-Weber Phakomatosis, Subacute Necrotizing Encephalomyelopathy, Subacute Necrotizing Encephalomyelopathy, Subacute Spongiform Encephalopathy, Subacute Necrotizing Encephalopathy, Subacute Sarcoidosis, Subacute Neuronopathic, Subaortic Stenosis, Subcortical Arteriosclerotic Encephalopathy, Subendocardial Sclerosis, Succinylcholine Sensitivity, Sucrase-Isomaltase Deficiency Congenital, Sucrose-Isomaltose Malabsorption Congenital, Sucrose Intolerance Congenital, Sudanophilic Leukodystrophy ADL, Sudanophilic Leukodystrophy Pelizaeus-Merzbacher Type, Sudanophilic Leukodystrophy Included, Sudden Infant Death Syndrome, Sudeck's Atrophy, Sugio-Kajii Syndrome, Summerskill Syndrome, Summit Acrocephalosyndactyly, Summitt's Acrocephalosyndactyly, Summitt Syndrome, Superior Oblique Tendon Sheath Syndrome, Suprarenal glands, Supravalvular Aortic Stenosis, Supraventricular tachycardia,

Surdicardiac Syndrome, Surdocardiac Syndrome, SVT, Sweat Gland Abscess, Sweating Gustatory Syndrome, Sweet Syndrome, Swiss Cheese Cartilage Syndrome, Syndactylic Oxycephaly, Syndactyly Type I with Microcephaly and Mental Retardation, Syndromatic Hepatic Ductular Hypoplasia, Syringomyelia, Systemic Aleukemic Reticuloendotheliosis, Systemic Amyloidosis, Systemic Carnitine Deficiency, Systemic Elastorrhexis, Systemic Lupus Erythematosus, Systemic Mast Cell Disease, Systemic Mastocytosis, Systemic-Onset Juvenile Arthritis, Systemic Sclerosis, Systopic Spleen, T-Lymphocyte Deficiency, Tachyalimentation Hypoglycemia, Tachycardia, Takahara syndrome, Takayasu Disease, Takayasu Arteritis, Talipes Calcaneus, Talipes Equinovarus, Talipes Equinus, Talipes Varus, Talipes Valgus, Tandem Spinal Stenosis, Tangier Disease, Tapetoretinal Degeneration, TAR Syndrome, Tardive Dystonia, Tardive Muscular Dystrophy, Tardive Dyskinesia, Tardive Oral Dyskinesia, Tardive Dyskinesia, Tardive Dystonia, Tardy Ulnar Palsy, Target Cell Anemia, Tarsomegaly, Tarui Disease, TAS Midline Defects Included, TAS Midline Defect, Tay Sachs Sphingolipidosis, Tay Sachs Disease, Tay Syndrome Ichthyosis, Tay Sachs Sphingolipidosis, Tay Syndrome Ichthyosis, Taybi Syndrome Type I, Taybi Syndrome, TCD, TCOF1, TCS, TD, TDO Syndrome, TDO-I, TDO-II, TDO-III, Telangiectasis, Telecanthus With Associated Abnormalities, Telecanthus-Hypospadias Syndrome, Temporal Lobe Epilepsy; Temporal Arteritis/Giant Cell Arteritis, Temporal Arteritis, TEN, Tendon Sheath Adherence Superior Obliqu, Tension Myalgia, Terminal Deletion of 4q Included, Terrian Corneal Dystrophy, Teschler-Nicola/Killian Syndrome, Tethered Spinal Cord Syndrome, Tethered Cord Malformation Sequence, Tethered Cord Syndrome, Tethered Cervical Spinal Cord Syndrome, Tetrahydrobiopterin Deficiencies, Tetrahydrobiopterin Deficiencies, Tetralogy of Fallot, Tetraphocomelia-Thrombocytopenia Syndrome, Tetrasomy Short Arm of Chromosome 9, Tetrasomy 9p, Tetrasomy Short Arm of Chromosome 18, Thalamic Syndrome, Thalamic Pain Syndrome, Thalamic Hyperesthetic Anesthesia, Thalassemia Intermedia, Thalassemia Minor, Thalassemia Major, Thiamine Deficiency, Thiamine-Responsive Maple Syrup Urine Disease, Thin-Basement-Membrane Nephropathy, Thiolase deficiency,RCDP,Acyl-CoA dihydroxyacetonephosphate acyltransferase, Third and Fourth Pharyngeal Pouch Syndrome, Third Degree Congenital (Complete) Heart Block, Thomsen Disease, Thoracic-Pelvic-Phalangeal Dystrophy, Thoracic Spinal Canal, Thoracoabdominal Syndrome,

Thoracoabdominal Ectopia Cordis Syndrome, Three M Syndrome, Three-M Slender-Boned Nanism, Thrombasthenia of Glanzmann and Naegeli, Thrombocythemia Essential, Thrombocytopenia-Absent Radius Syndrome, Thrombocytopenia-Hemangioma Syndrome, Thrombocytopenia-Absent Radii Syndrome, Thrombophilia Hereditary Due to AT III, Thrombotic Thrombocytopenic Purpura, Thromboulcerative Colitis, Thromboulcerative Colitis, Thymic Dysplasia with Normal Immunoglobulins, Thymic Agenesis,Thymic Aplasia DiGeorge Type, Thymic Hypoplasia Agammaglobulinemias Primary Included, Thymic Hypoplasia DiGeorge Type, Thymus Congenital Aplasia, Tic Douloureux, Tics, Tinel's syndrome, Tolosa Hunt Syndrome, Tonic Spasmodic Torticollis, Tonic Pupil Syndrome, Tooth and Nail Syndrome, Torch Infection, TORCH Syndrome, Torsion Dystonia, Torticollis, Total Lipodystrophy, Total anomalous pulmonary venous connection, Touraine's Aphthosis, Tourette Syndrome, Tourette's disorder, Townes-Brocks Syndrome, Townes Syndrome, Toxic Paralytic Anemia, Toxic Epidermal Necrolysis, Toxopachyosteose Diaphysaire Tibio-Peroniere, Toxopachyosteose, Toxoplasmosis Other Agents Rubella Cytomegalovirus Herpes Simplex, Tracheoesophageal Fistula with or without Esophageal Atresia, Tracheoesophageal Fistula, Transient neonatal myasthenia gravis, Transitional Atrioventricular Septal Defect, Transposition of the great arteries, Transtelephonic Monitoring, Transthyretin Methionine-30 Amyloidosis (Type I), Trapezoidocephaly-Multiple Synostosis Syndrome, Treacher Collins Syndrome, Treacher Collins-Franceschetti Syndrome 1, Trevor Disease, Triatrial Heart, Tricho-Dento-Osseous Syndrome, Trichodento Osseous Syndrome, Trichopoliodystrophy, Trichorhinophalangeal Syndrome, Trichorhinophalangeal Syndrome, Tricuspid atresia, Trifunctional Protein Deficiency, Trigeminal Neuralgia, Triglyceride Storage Disease Impaired Long-Chain Fatty Acid Oxidation, Trigonitis, Trigonocephaly, Trigonocephaly Syndrome, Trigonocephaly "C" Syndrome, Trimethylaminuria, Triphalangeal Thumbs-Hypoplastic Distal Phalanges-Onychodystrophy, Triphalangeal Thumb Syndrome, Triple Symptom Complex of Behcet, Triple X Syndrome, Triplo X Syndrome, Triploid Syndrome, Triploidy, Triploidy Syndrome, Trismus-Pseudocamptodactyly Syndrome, Trisomy, Trisomy G Syndrome, Trisomy X, Trisomy 6q Partial, Trisomy 6q Syndrome Partial, Trisomy 9 Mosaic, Trisomy 9P Syndrome (Partial) Included, Trisomy 11q Partial, Trisomy 14 Mosaic, Trisomy 14

Mosaicism Syndrome, Trisomy 21 Syndrome, Trisomy 22 Mosaic, Trisomy 22 Mosaicism Syndrome, TRPS, TRPS1, TRPS2, TRPS3, True Hermaphroditism, Truncus arteriosus, Tryptophan Malabsorption, Tryptophan Pyrrolase Deficiency, TS, TTP, TTTS, Tuberous Sclerosis, Tubular Ectasia, Turcot Syndrome, Turner Syndrome, Turner-Kieser Syndrome, Turner Phenotype with Normal Chromosomes (Karyotype), Turner-Varny Syndrome, Turricephaly, Twin-Twin Transfusion Syndrome, Twin-to-Twin Transfusion Syndrome, Type A, Type B, Type AB, Type O, Type I Diabetes, Type I Familial Incomplete Male, Type I Familial Incomplete Male Pseudohermaphroditism, Type I Gaucher Disease, Type I (PCCA Deficiency), Type I Tyrosinemia, Type II Gaucher Disease, Type II Histiocytosis, Type II (PCCB Deficiency), Type II Tyrosinnemia, Type IIA Distal Arthrogryposis Multiplex Congenita, Type III Gaucher Disease, Type III Tyrosinemia, Type III Dentinogenesis Imperfecta, Typical Retinoschisis, Tyrosinase Negative Albinism (Type I), Tyrosinase Positive Albinism (Type II), Tyrosinemia type 1 acute form, Tyrosinemia type 1 chronic form, Tyrosinosis, UCE, Ulcerative Colitis, Ulcerative Colitis Chronic Non-Specific, Ulnar-Mammary Syndrome, Ulnar-Mammary Syndrome of Pallister, Ulnar Nerve Palsy, UMS, Unclassified FODs, Unconjugated Benign Bilirubinemia, Underactivity of Parathyroid, Unilateral Ichthyosiform Erythroderma with Ipsilateral Malformations Limb, Unilateral Chondromatosis, Unilateral Defect of Pectoralis Muscle and Syndactyly of the Hand, Unilateral Hemidysplasia Type, Unilateral Megalencephaly, Unilateral Partial Lipodystrophy, Unilateral Renal Agenesis, Unstable Colon, Unverricht Disease, Unverricht-Lundborg Disease, Unverricht-Lundborg-Laf Disease, Unverricht Syndrome, Upper Limb - Cardiovascular Syndrome (Holt-Oram), Upper Motor Neuron Disease, Upper Airway Apnea, Urea Cycle Defects or Disorders, Urea Cycle Disorder Arginase Type, Urea Cycle Disorder Arginino Succinase Type, Urea Cycle Disorders Carbamyl Phosphate Synthetase Type, Urea Cycle Disorder Citrullinemia Type, Urea Cycle Disorders N-Acetyl Glutamate Synthetase Type, Urea Cycle Disorder OTC Type, Urethral Syndrome, Urethro-Oculo-Articular Syndrome, Uridine Diphosphate Glucuronosyltransferase Severe Def. Type I, Urinary Tract Defects, Urofacial Syndrome, Uroporphyrinogen III cosynthase, Urticaria pigmentosa, Usher Syndrome, Usher Type I, Usher Type II, Usher Type III, Usher Type IV, Uterine Synechiae, Uoporphyrinogen I-synthase, Uveitis, Uveomeningitis Syndrome, V-CJD, VACTEL Association, VACTERL

Association, VACTERL Syndrome, Valgus Calcaneus, Valine Transaminase Deficiency, Valinemia, Valproic Acid, Valproate acid exposure, Valproic acid exposure, Valproic acid, Van Buren's Disease, Van der Hoeve-Habertsma-Waardenburg-Gauldi Syndrome, Variable Onset Immunoglobulin Deficiency Dysgammaglobulinemia, Variant Creutzfeldt-Jakob Disease (V-CJD), Varicella Embryopathy, Variegate Porphyria, Vascular Birthmarks, Vascular Dementia Binswanger's Type, Vascular Erectile Tumor, Vascular Hemophilia, Vascular Malformations, Vascular Malformations of the Brain, Vasculitis, Vasomotor Ataxia, Vasopressin-Resistant Diabetes Insipidus, Vasopressin-Sensitive Diabetes Insipidus, VATER Association, Vcf syndrome, Vcfs, Velocardiofacial Syndrome, VeloCardioFacial Syndrome, Venereal Arthritis, Venous Malformations, Ventricular Fibrillation, Ventricular Septal Defects, Congenital Ventricular Defects, Ventricular Septal Defect, Ventricular Tachycardia, Venual Malformations, VEOHD, Vermis Aplasia, Vermis Cerebellar Agenesis, Vernal Keratoconjunctivitis, Verruca, Vertebral Anal Tracheoesophageal Esophageal Radial, Vertebral Ankylosing Hyperostosis, Very Early Onset Huntington's Disease, Very Long Chain Acyl-CoA Dehydrogenase (VLCAD) Deficiency, Vestibular Schwannoma Neurofibromatosis, Vestibulocerebellar, Virchow's Oxycephaly, Visceral Xanthogranulomatosis, Visceral Xantho-Granulomatosis, Visceral Myopathy-External Ophthalmoplegia, Visceromegaly-Umbilical Hernia-Macroglossia Syndrome, Visual Amnesia, Vitamin A Deficiency, Vitamin B-1 Deficiency, Vitelline Macular Dystrophy, Vitiligo, Vitiligo Capitis, Vitreoretinal Dystrophy, VKC, VKH Syndrome, VLCAD, Vogt Syndrome, Vogt Cephalosyndactyly, Vogt Koyanagi Harada Syndrome, Vogt Koyanagi Harada Syndrome, Von Bechterew-Strumpell Syndrome, Von Eulenburg Paramyotonia Congenita, Von Frey's Syndrome, Von Gierke Disease, Von Hippel-Lindau Syndrome, Von Mikulicz Syndrome, Von Recklinghausen Disease, Von Willebrandt Disease, VP, Vrolik Disease (Type II), VSD, Vulgaris Type Disorder of Cornification, Vulgaris Type Ichthyosis, W Syndrome, Waardenburg Syndrome, Waardenburg-Klein Syndrome, Waardenburg Syndrome Type I (WS1), Waardenburg Syndrome Type II (WS2), Waardenburg Syndrome Type IIA (WS2A), Waardenburg Syndrome Type IIB (WS2B), Waardenburg Syndrome Type III (WS3), Waardenburg Syndrome Type IV (WS4), Waelsch's Syndrome, WAGR Complex, WAGR Syndrome, Waldenstroem's Macroglobulinemia, Waldenstrom's Purpura, Waldenstrom's Syndrome,

Waldmann Disease, Walker-Warburg Syndrome, Wandering Spleen, Warburg Syndrome, Warm Antibody Hemolytic Anemia, Warm Reacting Antibody Disease, Wartenberg Syndrome, WAS, Water on the Brain, Watson Syndrome, Watson-Alagille Syndrome, Waterhouse-Friderichsen syndrome, Waxy Disease, WBS, Weaver Syndrome, Weaver-Smith Syndrome, Weber-Cockayne Disease, Wegener's Granulomatosis, Weil Disease, Weil Syndrome, Weill-Marchesani, Weill-Marchesani Syndrome, Weill-Reyes Syndrome, Weismann-Netter-Stuhl Syndrome, Weissenbacher-Zweymuller Syndrome, Wells Syndrome, Wenckebach, Werdnig-Hoffmann disease, Werdnig-Hoffman Disease, Werdnig-Hoffman Paralysis, Werlhof's Disease, Werner Syndrome, Wernicke's (C) I Syndrome, Wernicke's aphasia, Wernicke-Korsakoff Syndrome, West Syndrome, Wet Beriberi, WHCR, Whipple's Disease, Whipple Disease, Whistling face syndrome, Whistling Face-Windmill Vane Hand Syndrome, White-Darier Disease, Whitnall-Norman Syndrome, Whorled nevoid hypermelanosis, WHS, Wieacker Syndrome, Wieacher Syndrome, Wieacker-Wolff Syndrome, Wiedmann-Beckwith Syndrome, Wiedemann-Rautenstrauch Syndrome, Wildervanck Syndrome, Willebrand-Juergens Disease, Willi-Prader Syndrome, Williams Syndrome, Williams-Beuren Syndrome, Wilms' Tumor, Wilms' Tumor-Aniridia-Gonadoblastoma-Mental Retardation Syndrome, Wilms Tumor Aniridia Gonadoblastoma Mental Retardation, Wilms' Tumor-Aniridia-Genitourinary Anomalies-Mental Retardation Syndrome, Wilms Tumor-Pseudohermaphroditism-Nephropathy, Wilms Tumor and Pseudohermaphroditism, Wilms Tumor-Pseuodohermaphroditism-Glomerulopathy, Wilson's Disease, Winchester Syndrome, Winchester-Grossman Syndrome, Wiskott-Aldrich Syndrome, Wiskott-Aldrich Type Immunodeficiency, Witkop Ectodermal Dysplasias, Witkop Tooth-Nail Syndrome, Wittmaack-Ekbom Syndrome, WM Syndrome, WMS, WNS, Wohlfart-Disease, Wohlfart-Kugelberg-Welander Disease, Wolf Syndrome, Wolf-Hirschhorn Chromosome Region (WHCR), Wolf-Hirschhorn Syndrome, Wolff-Parkinson-White syndrome, Wolff Parkinson White Syndrome, Wolfram Syndrome, Wolman Disease (Lysomal Acid Lypase Deficiency), Woody Guthrie's Disease, WPW Syndrome, Writer's Cramp, WS, WSS, WWS, Wyburn-Mason Syndrome, X-Linked Addison's Disease, X-linked Adrenoleukodystrophy (X-ALD), X-linked Adult Onset Spinobulbar Muscular Atrophy, X-linked Adult Spinal Muscular Atrophy, X-Linked Agammaglobulinemia with Growth

Hormone Deficiency, X-Linked Agammaglobulinemia, Lymphoproliferate X-Linked Syndrome, X-linked Cardiomyopathy and Neutropenia, X-Linked Centronuclear Myopathy, X-linked Copper Deficiency, X-linked Copper Malabsorption, X-Linked Dominant Conradi-Hunermann Syndrome, X-Linked Dominant Inheritance Agenesis of Corpus Callosum, X-Linked Dystonia-parkinsonism, X-Linked Ichthyosis, X Linked Ichthyosis, X-Linked Infantile Agammaglobulinemia, X-Linked Infantile Nectrotizing Encephalopathy, X-linked Juvenile Retinoschisis, X-linked Lissencephaly, X-linked Lymphoproliferative Syndrome, X-linked Mental Retardation-Clasped Thumb Syndrome, X-Linked Mental Retardation with Hypotonia, X-linked Mental Retardation and Macroorchidism, X-Linked Progressive Combined Variable Immunodeficiency, X-Linked Recessive Conradi-Hunermann Syndrome, X-Linked Recessive Severe Combined Immunodeficiency, X-Linked Retinoschisis, X-linked Spondyloepiphyseal Dysplasia, Xanthine Oxidase Deficiency (Xanthinuria Deficiency, Hereditary), Xanthinuria Deficiency, Hereditary (Xanthine Oxidase Deficiency), Xanthogranulomatosis Generalized, Xanthoma Tuberosum, Xeroderma Pigmentosum, Xeroderma Pigmentosum Dominant Type, Xeroderma Pigmentosum Type A I XPA Classical Form, Xeroderma Pigmentosum Type B II XPB, Xeroderma Pigmentosum Type E V XPE, Xeroderma Pigmentosum Type C III XPC, Xeroderma Pigmentosum Type D IV XPD, Xeroderma Pigmentosum Type F VI XPF, Xeroderma Pigmentosum Type G VII XPG, Xeroderma Pigmentosum Variant Type XP-V, Xeroderma-Talipes-and Enamel Defect, Xerodermic Idiocy, Xerophthalmia, Xerotic Keratitis, XLP, XO Syndrome, XP, XX Male Syndrome,Sex Reversal, XXXXX Syndrome, XXY Syndrome, XYY Syndrome, XYY Chromosome Pattern, Yellow Mutant Albinism, Yellow Nail Syndrome, YKL, Young Female Arteritis, Yunis-Varon Syndrome, YY Syndrome, Z-E Syndrome, Z- and -Protease Inhibitor Deficiency, Zellweger syndrome, Zellweger cerebro-hepato-renal syndrome, ZES, Ziehen-Oppenheim Disease (Torsion Dystonia), Zimmermann-Laband Syndrome, Zinc Deficiency Congenital, Zinsser-Cole-Engman Syndrome, ZLS, Zollinger-Ellison Syndrome.

In addition, other diseases and disorders which can be treated by the methods of the present invention are cancer and related conditions. Types of cancers contemplated include

ABL1 protooncogene, AIDS Related Cancers, Acoustic Neuroma, Acute Lymphocytic Leukaemia, Acute Myeloid Leukaemia, Adenocystic carcinoma, Adrenocortical Cancer, Agnogenic myeloid metaplasia, Alopecia, Alveolar soft-part sarcoma, Anal cancer, Angiosarcoma, Aplastic Anaemia, Astrocytoma, Ataxia-telangiectasia, Basal Cell Carcinoma (Skin), Bladder Cancer, Bone Cancers, Bowel cancer, Brain Stem Glioma, Brain and CNS Tumors, Breast Cancer, CNS tumors, Carcinoid Tumors, Cervical Cancer, Childhood Brain Tumors, Childhood Cancer, Childhood Leukaemia, Childhood Soft Tissue Sarcoma, Chondrosarcoma, Choriocarcinoma, Chronic Lymphocytic Leukaemia, Chronic Myeloid Leukaemia, Colorectal Cancers, Cutaneous T-Cell Lymphoma, Dermatofibrosarcoma-protuberans, Desmoplastic-Small-Round-Cell-Tumor, Ductal Carcinoma, Endocrine Cancers, Endometrial Cancer, Ependymoma, Esophageal Cancer, Ewing's Sarcoma, Extra-Hepatic Bile Duct Cancer, Eye Cancer, Eye: Melanoma, Retinoblastoma, Fallopian Tube cancer, Fanconi Anaemia, Fibrosarcoma, Gall Bladder Cancer, Gastric Cancer, Gastrointestinal Cancers, Gastrointestinal-Carcinoid-Tumor, Genitourinary Cancers, Germ Cell Tumors, Gestational-Trophoblastic-Disease, Glioma, Gynaecological Cancers, Haematological Malignancies, Hairy Cell Leukaemia, Head and Neck Cancer, Hepatocellular Cancer, Hereditary Breast Cancer, Histiocytosis, Hodgkin's Disease, Human Papillomavirus, Hydatidiform mole, Hypercalcemia, Hypopharynx Cancer, IntraOcular Melanoma, Islet cell cancer, Kaposi's sarcoma, Kidney Cancer, Langerhan's-Cell-Histiocytosis, Laryngeal Cancer, Leiomyosarcoma, Leukaemia, Li-Fraumeni Syndrome, Lip Cancer, Liposarcoma, Liver Cancer, Lung Cancer, Lymphedema, Lymphoma, Hodgkin's Lymphoma, Non-Hodgkin's Lymphoma, Male Breast Cancer, Malignant-Rhabdoid-Tumor-of-Kidney, Medulloblastoma, Melanoma, Merkel Cell Cancer, Mesothelioma, Metastatic Cancer, Mouth Cancer, Multiple Endocrine Neoplasia, Mycosis Fungoides, Myelodysplastic Syndromes, Myeloma, Myeloproliferative Disorders, Nasal Cancer, Nasopharyngeal Cancer, Nephroblastoma, Neuroblastoma, Neurofibromatosis, Nijmegen Breakage Syndrome, Non-Melanoma Skin Cancer, Non-Small-Cell-Lung-Cancer-(NSCLC), Ocular Cancers, Oesophageal Cancer, Oral cavity Cancer, Oropharynx Cancer, Osteosarcoma, Ovarian Cancer, Pancreas Cancer, Paranasal Cancer, Parathyroid Cancer, Parotid Gland Cancer, Penile Cancer, Peripheral-Neuroectodermal-Tumors, Pituitary Cancer, Polycythemia vera, Prostate Cancer, Rare-

cancers-and-associated-disorders, Renal Cell Carcinoma, Retinoblastoma, Rhabdomyosarcoma, Rothmund-Thomson Syndrome, Salivary Gland Cancer, Sarcoma, Schwannoma, Sezary syndrome, Skin Cancer, Small Cell Lung Cancer (SCLC), Small Intestine Cancer, Soft Tissue Sarcoma, Spinal Cord Tumors, Squamous-Cell-Carcinoma-(skin), Stomach Cancer, Synovial sarcoma, Testicular Cancer, Thymus Cancer, Thyroid Cancer, Transitional-Cell-Cancer-(bladder), Transitional-Cell-Cancer-(renal-pelvis-/-ureter), Trophoblastic Cancer, Urethral Cancer, Urinary System Cancer, Uroplakins, Uterine sarcoma, Uterus Cancer, Vaginal Cancer, Vulva Cancer, Waldenstrom's-Macroglobulinemia and Wilms' Tumor.

An "effective amount" means an amount necessary at least partly to attain the desired immune response, or to delay the onset or inhibit progression or halt altogether, the onset or progression of a particular condition of the individual to be treated, the taxonomic group of the individual to be treated, the degree of protection desired, the formulation of the vaccine, the assessment of the medical situation, and other relevant factors. It is expected that the amount will fall in a relatively broad range that can be determined through routine trials.

In accordance with these methods, AGT-106, AGT-113, AGT-201, AGT-202 and/or AGT-203 or *AGT-106, AGT-113, AGT-201, AGT-202* and/or *AGT-203* or agents capable of modulating the expression or activity of said molecules may be co-administered with one or more other compounds or other molecules. By "co-administered" is meant simultaneous administration in the same formulation or in two different formulations *via* the same or different routes or sequential administration by the same or different routes. By "sequential" administration is meant a time difference of from seconds, minutes, hours or days between the administration of the two types of molecules. These molecules may be administered in any order.

In yet another aspect, the present invention relates to the use of an agent capable of modulating the expression of *AGT-106, AGT-113, AGT-201, AGT-202* and/or *AGT-203* or a derivative, homolog or analog thereof in the manufacture of a medicament for the

treatment of a condition characterized by mitochondrial dysfunction, myopathy, genetic disorder or cancer.

In still yet another aspect, the present invention relates to the use of an agent capable of modulating the activity of AGT-106, AGT-113, AGT-201, AGT-202 and/or AGT-203 or a derivative, homolog, analog, chemical equivalent or mimetic thereof in the manufacture of a medicament for the treatment of a condition characterized by mitochondrial dysfunction, myopathy, genetic disorder or cancer.

A further aspect of the present invention relates to the use of *AGT-106, AGT-113, AGT-201, AGT-202* and/or *AGT-203* or derivative, homolog or analog thereof or AGT-106, AGT-113, AGT-201, AGT-202 and/or AGT-203 or derivative, homolog, analog, chemical equivalent or mimetic thereof in the manufacture of a medicament for the treatment of a condition characterized by mitochondrial dysfunction, myopathy, genetic disorder or cancer.

Still yet another aspect of the present invention relates to agents for use in modulating the expression of *AGT-106, AGT-113, AGT-201, AGT-202* and/or *AGT-203* or a derivative, homolog or analog thereof.

A further aspect relates to agents for use in modulating AGT-106, AGT-113, AGT-201, AGT-202 and/or AGT-203 activity or a derivative, homolog, analog, chemical equivalent or mimetic thereof.

Still another aspect of the present invention relates to AGT-106, AGT-113, AGT-201, AGT-202 and/or AGT-203 or derivative, homolog or analog thereof or AGT-106, AGT-113, AGT-201, AGT-202 and/or AGT-203 or derivative, homolog, analog, chemical equivalent or mimetic thereof for use in treating a condition characterized by one or more symptoms of mitochondrial dysfunction, myopathy, genetic disorder or cancer.

In a related aspect of the present invention, the mammal undergoing treatment may be a human or an animal in need of therapeutic or prophylactic treatment.

The terms "treating" and "treatment" as used herein refer to a reduction in the severity and/or frequency of symptoms associated with *inter alia* a mitochondrial dysfunction, myopathy, genetic disorder or cancer, elimination of symptoms and/or the underlying cause, prevention of the occurrence of symptoms of disease and/or the underlying cause and improvement or remediation of damage.

"Treating" a subject may involve prevention of the disorder or disease condition or adverse physiological event in a susceptible individual as well as treatment of a clinically symptomatic individual by inhibiting a disease or disorder. Generally, such conditions involve, weakness (which may be intermittent), neuropathic pain, absent reflexes, gastrointestinal problem (gastroesophogeal reflux, delayed gastric emptying, constipation, pseudo-obstruction), fainting, absent or excessive sweating resulting in temperature regulation problems weakness, hypotonia, cramping, muscle pain, proximal renal tubular wasting resulting in loss of protein, magnesium, phosphorous, calcium and other electrolytes, cardiac conduction defects (heart blocks) and cardiomyopathy, hypoglycemia (low blood sugar) and liver failure, visual loss and blindness, hearing loss and deafness, diabetes and exocrine pancreatic failure (inability to make digestive enzymes), mitochondrial dysfunction, including failure to gain weight, short statue, fatigue and respiratory problems.

Accordingly, the present invention contemplates in one embodiment a composition comprising a modulator of *AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203* expression or AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 activity and one or more pharmaceutically acceptable carriers and/or diluents. In another embodiment, the composition comprises *AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203* or a derivative, homolog, analog or mimetic thereof and one or more pharmaceutically acceptable carriers and/or diluents.

For brevity, all such components of such a composition are referred to as "active components".

The compositions of active components in a form suitable for injectable use include sterile aqueous solutions (where water soluble) and sterile powders for the extemporaneous preparation of sterile injectable solutions. In all cases, the form must be sterile and must be fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi.

The carrier can be a solvent or other medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol and liquid polyethylene glycol, and the like), suitable mixtures thereof, and vegetable oils.

The preventions of the action of microorganisms can be brought about by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thirmerosal and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars or sodium chloride. Prolonged absorption of the injectable compositions can be brought about by the use in the compositions of agents delaying absorption, for example, aluminum monostearate and gelatin.

Sterile injectable solutions are prepared by incorporating the active components in the required amount in the appropriate solvent with optionally other ingredients, as required, followed by sterilization by, for example, filter sterilization, irradiation or other convenient means. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and the freeze-drying technique which yield a powder of the active ingredient plus any additional desired ingredient from previously sterile-filtered solution thereof.

When *AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203* and AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 including AGT-106, AGT-113, AGT-201, AGT-202

and AGT-203 itself are suitably protected they may be orally administered, for example, with an inert diluent or with an assimilable edible carrier, or it may be enclosed in hard or soft shell gelatin capsule, or it may be compressed into tablets, or it may be incorporated directly with the food of the diet. For oral therapeutic administration, the active compound may be incorporated with excipients and used in the form of ingestible tablets, buccal tablets, troches, capsules, elixirs, suspensions, syrups, wafers, and the like. Such compositions and preparations should contain at least 1% by weight of active compound. The percentage of the compositions and preparations may, of course, be varied and may conveniently be between about 5 to about 80% of the weight of the unit. The amount of active compound in such therapeutically useful compositions is such that a suitable dosage will be obtained. Preferred compositions or preparations according to the present invention are prepared so that an oral dosage unit form contains between about 0.1 μg and 2000 mg of active compound.

The tablets, troches, pills, capsules and the like may also contain the following: A binder such as gum tragacanth, acacia, corn starch or gelatin; excipients such as dicalcium phosphate; a disintegrating agent such as corn starch, potato starch, alginic acid and the like; a lubricant such as magnesium stearate; and a sweetening agent such a sucrose, lactose or saccharin may be added or a flavouring agent such as peppermint, oil of wintergreen, or cherry flavouring. When the dosage unit form is a capsule, it may contain, in addition to materials of the above type, a liquid carrier. Various other materials may be present as coatings or to otherwise modify the physical form of the dosage unit. For instance, tablets, pills, or capsules may be coated with shellac, sugar or both. A syrup or elixir may contain the active compound, sucrose as a sweetening agent, methyl and propylparabens as preservatives, a dye and flavouring such as cherry or orange flavour. Of course, any material used in preparing any dosage unit form should be pharmaceutically pure and substantially non-toxic in the amounts employed. In addition, the active compound may be incorporated into sustained-release preparations and formulations.

Pharmaceutically acceptable carriers and/or diluents include any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption

delaying agents and the like. The use of such media and agents for pharmaceutical active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active ingredient, use thereof in the therapeutic compositions is contemplated. Supplementary active ingredients can also be incorporated into the compositions.

It is especially advantageous to formulate parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the mammalian subjects to be treated; each unit containing a predetermined quantity of active material calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the novel dosage unit forms of the invention are dictated by and directly dependent on (a) the unique characteristics of the active material and the particular therapeutic effect to be achieved, and (b) the limitations inherent in the art of compounding such an active material for the treatment of disease in living subjects having a diseased condition in which bodily health is impaired as herein disclosed in detail.

The principal active component may be compounded for convenient and effective administration in sufficient amounts with a suitable pharmaceutically acceptable carrier in dosage unit form. A unit dosage form can, for example, contain the principal active component in amounts ranging from 0.5 μg to about 2000 mg. Expressed in proportions, the active compound is generally present in from about 0.5 μg to about 2000 mg/ml of carrier. In the case of compositions containing supplementary active ingredients, the dosages are determined by reference to the usual dose and manner of administration of the said ingredients.

In general terms, effective amounts of AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 will range from 0.01 ng/kg/body weight to above 10,000 mg/kg/body weight. Alternative amounts range from 0.1 ng/kg/body weight is above 1000 mg/kg/body weight. AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 may be administered per minute, hour, day, week, month or year depending on the condition being treated. The route of

administration may vary and includes intravenous, intraperitoneal, sub-cutaneous, intramuscular, intranasal, *via* suppository, *via* infusion, *via* drip, orally or *via* other convenient means.

The pharmaceutical composition may also comprise genetic molecules such as a vector capable of transfecting target cells where the vector carries a nucleic acid molecule capable of modulating *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203* expression or AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 activity. The vector may, for example, be a viral vector.

Still another aspect of the present invention is directed to antibodies to AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 and their derivatives and homologs. Such antibodies may be monoclonal or polyclonal and may be selected from naturally occurring antibodies to AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 or may be specifically raised to AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 or derivatives or homologs thereof. In the case of the latter, AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 or their derivatives or homologs may first need to be associated with a carrier molecule. The antibodies and/or recombinant AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 or their derivatives of the present invention are particularly useful as therapeutic or diagnostic agents. Antibodies to AGT-203, for example, are particularly useful to monitor the levels of AGT-203. In this regard, enhanced levels of AGT-203 are noted in cervical cancer tissue and decreased levels of AGT-203 are noted in tissue from kidney, breast and pancreatic cancer.

AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 and their derivatives can be used to screen for naturally occurring antibodies to AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 which may occur in certain autoimmune diseases or where cell death is occurring. These may occur, for example in some autoimmune diseases. Alternatively, specific antibodies can be used to screen for AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203. Techniques for such assays are well known in the art and include, for example, sandwich assays and ELISA.

Antibodies to AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 of the present invention may be monoclonal or polyclonal and may be selected from naturally occurring antibodies to the AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 or may be specifically raised to the AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 or their derivatives. In the case of the latter, the AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 protein may need first to be associated with a carrier molecule. Alternatively, fragments of antibodies may be used such as Fab fragments. Furthermore, the present invention extends to recombinant and synthetic antibodies and to antibody hybrids. A "synthetic antibody" is considered herein to include fragments and hybrids of antibodies. The antibodies of this aspect of the present invention are particularly useful for immunotherapy and may also be used as a diagnostic tool or as a means for purifying AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203.

For example, specific antibodies can be used to screen for AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 proteins. The latter would be important, for example, as a means for screening for levels of AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 in a cell extract or other biological fluid or purifying AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 made by recombinant means from culture supernatant fluid. Techniques for the assays contemplated herein are known in the art and include, for example, sandwich assays and ELISA.

It is within the scope of this invention to include any second antibodies (monoclonal, polyclonal or fragments of antibodies) directed to the first mentioned antibodies discussed above. Both the first and second antibodies may be used in detection assays or a first antibody may be used with a commercially available anti-immunoglobulin antibody. An antibody as contemplated herein includes any antibody specific to any region of AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203.

Both polyclonal and monoclonal antibodies are obtainable by immunization with the enzyme or protein and either type is utilizable for immunoassays. The methods of

obtaining both types of sera are well known in the art. Polyclonal sera are less preferred but are relatively easily prepared by injection of a suitable laboratory animal with an effective amount of AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203, or antigenic parts thereof, collecting serum from the animal, and isolating specific sera by any of the known immunoadsorbent techniques. Although antibodies produced by this method are utilizable in virtually any type of immunoassay, they are generally less favoured because of the potential heterogeneity of the product.

The use of monoclonal antibodies in an immunoassay is particularly preferred because of the ability to produce them in large quantities and the homogeneity of the product. The preparation of hybridoma cell lines for monoclonal antibody production derived by fusing an immortal cell line and lymphocytes sensitized against the immunogenic preparation can be done by techniques which are well known to those who are skilled in the art. (See, for example, Douillard and Hoffman, Basic Facts about Hybridomas, in *Compendium of Immunology* Vol. II, ed. by Schwartz, 1981; Kohler and Milstein, *Nature 256:* 495-499, 1975; Kohler and Milstein, *European Journal of Immunology 6:* 511-519, 1976).

Another aspect of the present invention contemplates a method for detecting AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 or a derivative or homolog thereof in a biological sample from a subject, said method comprising contacting said biological sample with an antibody specific for AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 or their antigenic derivatives or homologs for a time and under conditions sufficient for a complex to form, and then detecting said complex.

The presence of the complex is indicative of the presence of AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203. This assay may be quantitated or semi-quantitated to determine a propensity to develop mitochondrial dysfunction, myopathy, genetic disorder or cancer or to monitor a therapeutic regimine.

The presence of AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 may be accomplished in a number of ways such as by Western blotting and ELISA procedures. A

wide range of immunoassay techniques are available as can be seen by reference to U.S. Patent Nos. 4,016,043, 4,424,279 and 4,018,653. These, of course, includes both single-site and two-site or "sandwich" assays of the non-competitive types, as well as in the traditional competitive binding assays. These assays also include direct binding of a labeled antibody to a target.

Sandwich assays are among the most useful and commonly used assays. A number of variations of the sandwich assay technique exist, and all are intended to be encompassed by the present invention. Briefly, in a typical forward assay, an unlabeled antibody is immobilized on a solid substrate and the sample to be tested brought into contact with the bound molecule. After a suitable period of incubation, for a period of time sufficient to allow formation of an antibody-AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 complex, a second antibody specific to the AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203, labeled with a reporter molecule capable of producing a detectable signal, is then added and incubated, allowing time sufficient for the formation of another complex of antibody-AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203-labeled antibody. Any unreacted material is washed away, and the presence of AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 is determined by observation of a signal produced by the reporter molecule. The results may either be qualitative, by simple observation of the visible signal, or may be quantitated by comparing with a control sample containing known amounts of hapten. Variations on the forward assay include a simultaneous assay, in which both sample and labeled antibody are added simultaneously to the bound antibody. These techniques are well known to those skilled in the art, including any minor variations as will be readily apparent. In accordance with the present invention, the sample is one which might contain AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 including cell extract, tissue biopsy or possibly serum, saliva, mucosal secretions, lymph, tissue fluid and respiratory fluid. The sample is, therefore, generally a biological sample comprising biological fluid but also extends to fermentation fluid and supernatant fluid such as from a cell culture.

The solid surface is typically glass or a polymer, the most commonly used polymers being cellulose, polyacrylamide, nylon, polystyrene, polyvinyl chloride or polypropylene. The solid supports may be in the form of tubes, beads, discs of microplates, or any other surface suitable for conducting an immunoassay. The binding processes are well-known in the art and generally consist of cross-linking covalently binding or physically adsorbing, the polymer-antibody complex is washed in preparation for the test sample. An aliquot of the sample to be tested is then added to the solid phase complex and incubated for a period of time sufficient (e.g. 2-40 minutes or overnight if more convenient) and under suitable conditions (e.g. from room temperature to about 37°C) to allow binding of any subunit present in the antibody. Following the incubation period, the antibody subunit solid phase is washed and dried and incubated with a second antibody specific for a portion of AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203. The second antibody is linked to a reporter molecule which is used to indicate the binding of the second antibody to AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203.

An alternative method involves immobilizing the target molecules in the biological sample and then exposing the immobilized target to specific antibody which may or may not be labeled with a reporter molecule. Depending on the amount of target and the strength of the reporter molecule signal, a bound target may be detectable by direct labeling with the antibody. Alternatively, a second labeled antibody, specific to the first antibody is exposed to the target-first antibody complex to form a target-first antibody-second antibody tertiary complex. The complex is detected by the signal emitted by the reporter molecule.

By "reporter molecule" as used in the present specification, is meant a molecule which, by its chemical nature, provides an analytically identifiable signal which allows the detection of antigen-bound antibody. Detection may be either qualitative or quantitative. The most commonly used reporter molecules in this type of assay are either enzymes, fluorophores or radionuclide containing molecules (i.e. radioisotopes) and chemiluminescent molecules.

In the case of an enzyme immunoassay, an enzyme is conjugated to the second antibody, generally by means of glutaraldehyde or periodate. As will be readily recognized, however,

a wide variety of different conjugation techniques exist, which are readily available to the skilled artisan. Commonly used enzymes include horseradish peroxidase, glucose oxidase, ß-galactosidase and alkaline phosphatase, amongst others. The substrates to be used with the specific enzymes are generally chosen for the production, upon hydrolysis by the corresponding enzyme, of a detectable colour change. Examples of suitable enzymes include alkaline phosphatase and peroxidase. It is also possible to employ fluorogenic substrates, which yield a fluorescent product rather than the chromogenic substrates noted above. In all cases, the enzyme-labeled antibody is added to the first antibody hapten complex, allowed to bind, and then the excess reagent is washed away. A solution containing the appropriate substrate is then added to the complex of antibody-antigen-antibody. The substrate will react with the enzyme linked to the second antibody, giving a qualitative visual signal, which may be further quantitated, usually spectrophotometrically, to give an indication of the amount of hapten which was present in the sample. A "reporter molecule" also extends to use of cell agglutination or inhibition of agglutination such as red blood cells on latex beads, and the like.

Alternately, fluorescent compounds, such as fluorecein and rhodamine, may be chemically coupled to antibodies without altering their binding capacity. When activated by illumination with light of a particular wavelength, the fluorochrome-labeled antibody adsorbs the light energy, inducing a state to excitability in the molecule, followed by emission of the light at a characteristic colour visually detectable with a light microscope. As in the EIA, the fluorescent labeled antibody is allowed to bind to the first antibody-hapten complex. After washing off the unbound reagent, the remaining tertiary complex is then exposed to the light of the appropriate wavelength the fluorescence observed indicates the presence of the hapten of interest. Immunofluorescene and EIA techniques are both very well established in the art and are particularly preferred for the present method. However, other reporter molecules, such as radioisotope, chemiluminescent or bioluminescent molecules, may also be employed.

The present invention also contemplates genetic assays such as involving PCR analysis to detect *AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203* or their derivatives. For

example, differential expression of AGT-203 can be used to detect or diagnose a particular cancer. In this regard, AGT-203 expression is up-regulated in cervical cancer and down-regulated in cancers of the kidney, breast and pancreas.

Accordingly, the present invention contemplates methods and agents to screen for variants, polymorphosims or mutations in any one of *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203* which would provide an indication of an abnormality leading to a disease or condition contemplated herein.

The term "variant", "polymorphism" or "mutation" refers to a difference in a DNA or RNA sequence or sequences among individuals, groups or populations which give rise to a statistically significant phenotype or physiological condition or the ability to be a carrier for a genetic predisposition for the development of the condition. Examples of genetic polymorphisms include mutations that result by chance or are induced by external features. These polymorphisms or mutations may be indicative of a disease or disorder and may arise following a genetic disease, a chromosomal abnormality, a genetic predisposition, a viral infection, a fungal infection, a bacterial infection or a protist infection or following chemotherapy, radiation therapy or substance abuse including alcohol or drug abuse. The polymorphisms may also dictate or contribute to symptoms of cancer or a related condition or a pre-cancerous condition. In a preferred aspect, the variants of the present invention are indicative of a diagnosing or detecting cancer or a related condition or a pre-cancerous condition in an individual or group of individuals or the predisposition of developing same or the ability to be a carrier for a genetic predisposition for the development of such condition.

Examples of nucleotide changes contemplated herein include single nucleotide polymorphisms (SNPs), multiple nucleotide polymorphisms (MNPs), frame shift mutations, including insertions and deletions (also called deletion insertion polymorphisms or DIPS), nucleotide substitutions, nonsense mutations as well as truncations.

Reference hereto to "cancer" refers to a disorder characteriszed by any malignant growth or tumor caused by abnormal and uncontrolled cell division. The term "cancer" includes solid tumors and metastatic cancers as well as a range of leukemias. A condition "related" to cancer includes a range of inflammatory conditions which although not traditionally identified as a "cancer have symptoms, aetiologies and prognoses similar to cancer. Cancers of particular interest include, but are not limited to, are cancers of the cervix, kidney, breast and pancreas.

Any number of methods may be used to calculate the statistical significance of a variant and its association with a cancer or related condition or a pre-cancerous condition. Particular statistical analysis methods which may be used are described in Fisher and vanBelle, "*Biostatistics: A Methodology for the Health Sciences*" Wiley-Intersciences (New York) 1993. This analysis may also include a regression calculation of which variant sites in one or more of *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203* give the most significant contribution to the development of disease or condition. One regression model useful in the instant the invention starts with a model of the form

$$r = r_0 + (S \times d)$$

where r is the response, r_0 is a constant called the "intercept", S is the slope and d is the dose. To determine the dose, the most-common and least common nucleotides at the variant site are first defined. Then, for each individual in the trial population, one calculates a "dose" as the number of least-common nucleotides the individual has at the variant site of interest. This value can be 0 (homozygous for the least-common nucleotide), 1 (heterozygous), or 2 (homozygous for the most common nucleotide). An individual's "response" is the value of the clinical measurement. Standard linear regression methods are then used to fit all the individuals' doses and responses to a single model (see e.g. Fisher and vanBelle, *supra*, Ch 9). The outputs of the regression calculation are the intercept r_0, the slope S, and the variance (which measures how well the data fits this simple linear model). The Students t-test value and the level of significance can then be calculated for each of the variant sites.

A cancer or a related condition or a pre-cancerous condition or any other condition contemplated herein or the predisposition of developing same or the ability to be a carrier for a genetic predisposition for the development of such a condition involving one or mor of *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203* may be ascertained by screening any tissue from an individual for genetic material carrying these genetic loci for the presence of a variant including a variant which is associated with a particular condition. Most conveniently screening is performed using blood which is drawn and DNA extracted from the cells of the blood. In addition, prenatal diagnosis can be accomplished by testing fetal cells, placental cells or amniotic cells for a polymorphism or variant in one or more of *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203.* Alternatively, biopsies can be taken and DNA extracted.

In yet another alternative, internal diagnostic analyses are conducted using internal probes, sensors, catheters and the like which are inserted by a specialist clinician to collect and/or read a sample which is then recorded optically or by electrical impulse and analysed by a computer.

Accordingly, another aspect of the present invention contemplates a method for diagnosing a disease or condition as herein defined or the predisposition of developing same or the ability to be a carrier for a genetic predisposition for the development of such a condition in an individual, said method comprising obtaining or extracting DNA sample from cells of said individual and screening for or otherwise detecting the presence of a genetic variation in one or more of *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203* including its 5' or 3' terminal region, promoters, introns or exons with a statistically significant association with a particular diseases or conditions

The genetic test can be part of an overall diagnostic protocol involving medical tests. Consequently, this aspect of the present invention may be considered as a confirmatory test or part of a series of tests in the final diagnosis of a disease or condition or the ability to be a carrier for a genetic predisposition for the development of cancer.

There are many methods which may be used to detect a DNA sequence profile. Direct DNA sequencing, either manual sequencing or automated fluorescent sequencing can detect sequence variation including a polymorphism or mutation. Another approach is the single-stranded conformation polymorphism assay (SSCP) (Orita, *et al.*, *Proc. Natl. Acad. Sci. USA. 86*:2766-2770, 1989). This method does not detect all sequence changes, especially if the DNA fragment size is greater than 200 bp, but can be optimized to detect most DNA sequence variation. The reduced detection sensitivity is a disadvantage, but the increased throughput possible with SSCP makes it an attractive, viable alternative to direct sequencing for mutation detection. The fragments which have shifted mobility on SSCP gels are then sequenced to determine the exact nature of the DNA sequence variation.

Other approaches based on the detection of mismatches between the two complementary DNA strands include clamped denaturing gel electrophoresis (CDGE) (Sheffield *et al. Proc. Natl. Acad. Sci. USA 86*:232-236, 1989), heteroduplex analysis (HA) (White *et al. Genomics 12*:301-306, 1992) and chemical mismatch cleavage (CMC) (Grompe *et al. Proc. Natl. Acad. Sci. USA 86*:5855-5892, 1989). None of the methods described above detects large deletions, duplications or insertions, nor will they detect a mutation in a regulatory region or a gene. Other methods which would detect these classes of mutations include a protein truncation assay or the asymmetric assay. A review of currently available methods of detecting DNA sequence variation can be found in Kwok (*Curr Issues Mol. Biol. 5(2)*:43-60, 2003, Twyman and Primrose, *Pharmacogenomics. 4(1)*:67-79, 2003, Edwards and Bartlett, *Methods Mol. Biol. 226*:287-294, 2003 and Brennan, *Am. J. Pharmacogenomics. 1(4)*:395-302, 2001). Once a mutation is known, an allele-specific detection approach such as allele-specific oligonucleotide (ASO) hybridization can be utilized to rapidly screen large numbers of other samples for that same mutation. Such a technique can utilize probes which are labeled with gold nanoparticles or any other reporter molecule to yield a visual color result (Elghanian *et al. Science 277*:1078-1081, 1997).

Methods for a more complete, yet still indirect, test for confirming the presence of a susceptibility allele include: 1) single-stranded conformation analysis (SSCP) (Orita *et al.*, 1989: *supra)*; 2) denaturing gradient gel electrophoresis (DGGE) (Wartell *et al. Nucl. Acids Res. 18*:2699-2705, 1990; Sheffield *et al.* 1989 *supra*); 3) RNase protection assays (Finkelstein *et al. Genomics 7*:167-172, 1990; Kinszler *et al. Science 251*:1366-1370, 1991); 4) allele-specific oligonucleotides [ASOs] (Conner *et al. Proc. Natl. Acad. Sci. USA 80*:278-282, 1983); 5) the use of proteins which recognize nucleotide mismatches, such as the *E. coli* mutS protein (Modrich *Ann. Rev. Genet. 25*:229-253, 1991); 6) allele-specific PCR (Ruano and Kidd *Nucl. Acids Res. 17*:8392, 1989); and 7) PCR amplification of the site of the polymorphism followed by digestion using a restriction endonuclease that cuts or fails to cut when the variant allele is present.

Additionally, real-time PCR may be included such as the allele specific kinetic real-time PCR assay can be used or allele specific real-time TaqMan probes.

For allele-specific PCR, primers are used which hybridize to a portion of one or more of *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203*. If the particular variant is not present, an amplification product is not observed. Amplification Refractory Mutation System (ARMS) can also be used, as disclosed in European Patent Application Publication No. 0332435. Insertions and deletions of genes can also be detected by cloning, sequencing and amplification. In addition, restriction fragment length polymorphism (RFLP) probes for the gene or surrounding marker genes can be used to score alteration of an allele or an insertion in a polymorphic fragment. Such a method is particularly useful for screening relatives of an affected individual for the presence of the mutation found in that individual. Other techniques for detecting insertions and deletions as known in the art can be used.

The assays of the present invention may also extend to measuring *AGT-106, AGT-113, AGT-201, AGT-202* and *AGT-203* or AGT-106, AGT-113, AGT-201, AGT-202 and AGT-203 in association with another gene or molecule.

The present invention is further described by the following non-limiting Examples.

EXAMPLE 1

Psammomys obesus colony

A *Psammomys obesus* colony is maintained at Deakin University, Waurn Ponds, Geelong, Victoria, Australia with the breeding pairs fed *ad libitum* a diet of lucerne and standard laboratory chow. Animals are weaned at four weeks of age and sustained on a diet of standard laboratory chow from which 12% of energy was derived from fat, 63% from carbohydrate and 25% from protein (Barastoc, Pakenham, Australia). Animals are housed in a humidity and temperature controlled room (22 ± 1°C) with a 12-12-hour light-dark cycle.

Group A animals are lean, normoglycemic and normoinsulinemic, group B animals are obese, normoglycemic and hyperinsulinemic, and group C animals are obese, hyperglycemic and hyperinsulinemia.

EXAMPLE 2

Experimental animals

At 18 weeks of age the animals were weighed and blood collected from the tail vein in the fed state. The animals were sacrificed and the tissues immediately removed, weighed, frozen in liquid nitrogen and stored at -80°C. Percent body fat was estimated from the combined weight of mesenteric, suprascapular, perirenal, epididymal and intramuscular (from between the heads of gastrocnemius) fat pads expressed as a percentage of total body weight. Animals were classified into groups A, B or C based on their blood glucose and insulin concentrations. The cut-off values for hyperglycemia and hyperinsulinemia were 8 mmol/L and 150 μU/ml respectively. The fasted animals were weighed and bled in the fed state then fasted for 24 hours, before being weighed and bled again before sacrifice.

EXAMPLE 3

Analytical methods

Whole blood glucose was measured immediately using an enzymatic glucose analyser (Model 27, Yellow Springs Instruments, OH). Plasma insulin concentrations were determined using a double antibody solid phase radioimmunoassay (Phadeseph, Kabi Pharmacia Diagnostics, Sweden).

EXAMPLE 4

RNA extraction and reverse transcription

RNA was extracted from tissues using TriZol (Life Technologies, Rockville, MD) according to manufacturer's recommendations for each tissue type. RNA was quantitated by spectrophotometry at 260 nm (Beckman Instruments, Fullerton, CA) and 2 μg electrophoresed through a 1% w/v glyoxal agarose gel (Ambion, Austin, TX) to check the integrity. The RNA was then reverse transcribed using AMV reverse transcriptase with oligo(dT) primers (Promega, Madison, WI).

EXAMPLE 5

Statistical analysis

All data are expressed as mean ± S.E.M. A one-way analysis of variance in combination with *post hoc* least significant difference or Games-Howell test were used to compare means between groups, and t-tests were used where appropriate. A 2-tailed Pearson correlation was performed to analyse relationships between gene expression and phenotypes. Blood glucose and plasma insulin concentrations were log transformed prior to analysis to approximate a normal distribution. Differences were considered significant at $P<0.05$.

EXAMPLE 6

Differential Display PCR

RNA was extracted from tissues using TriZol (Life Technologies, Rockville, MD) and DNase-treated (Life Technologies), phenol:chloroform (4:1) extracted and ethanol precipitated. RNA was quantitated by spectrophotometry at 260 nm (Beckman Instruments, Fullerton, CA) and 2 µg electrophoresed through a 1% w/v glyoxal agarose gel (Ambion, Austin, TX) to check the integrity. The RNA was then reverse transcribed using Superscript II reverse transcriptase (Life Technologies) with anchored oligo(dT) primers. Differential display PCR was performed on hypothalamic cDNA samples from obese and lean *Psammomys obesus* in the fed and fasted state using an RNAimage mRNA Differential Display System (GenHunter Corporation, Nashville, Tennessee). The PCR products were separated on a 6% w/v polyacrylamide gel, and differentially expressed PCR fragments were visualized by exposing the dried gel to x-ray film. Candidate bands were excised from the gel and reamplified by PCR using the appropriate primer combination. Sequencing reactions were carried out using ABI PRISM Big-Dye terminator cycle sequencing ready reaction kits and analyzed on an ABI 373A DNA sequencer. Gene database searches were performed at the National Centre for Biotechnology Information using the BLAST network service.

EXAMPLE 7

Macroarray

RNA was extracted from tissues using TriZol (Life Technologies, Rockville, MD) and DNase-treated (Life Technologies), phenol:chloroform (4:1) extracted and ethanol precipitated. RNA was quantitated by spectrophotometry at 260 nm (Beckman Instruments, Fullerton, CA) and 2 µg electrophoresed through a 1% w/v glyoxal agarose gel (Ambion, Austin, TX) to check the integrity. Pooled RNA samples for each of the study groups were labeled with ^{33}P d-ATP, and hybridiszd to human GF 201 membrane microarray filters (Research Genetics). The membrane was spotted with a total of 5184 genes, including known genes and expressed sequence tags. The level of binding to each

gene was quantitated using a phosphorimager and compared using Pathways software (Research Genetics).

EXAMPLE 8

AGT-106

AGT-106 was identified as being differentially expressed using the technique of differential display PCR in the hypothalamus of the Israeli Sand Rat (ISR) and expression of AGT-106 was higher in fed compared to fasted Sand rats.

Primers used were:-

AGT-106:

Forward primer: 5'-CAATCACCGCTTTTAAGATAGTTTGT-3' [SEQ ID NO:12]

Reverse primer: 5'-AGCATTAAAAAGGGCTCGCA-3' [SEQ ID NO:13]

The partial nucleotide sequence of *Psammomys obesus* AGT-106 cDNA is as follows:-

NTTTGNTGNCCNGCTGTGTGTGTTAGAAGAAAACAGAAAAGGAAAGAAAAACAATCACCGC
TTTTAAGATAGTTTGTATCAGCTTAGATTTCATCATGACTGTTTTACATACTGGAATTTAT
AAATTGTAAGTTATCATTTTCCAATGCGAGCCCTTTTTAATGCTTTTTAAAACTTGTGAAT
AAAATTGATACTCCTT [SEQ ID NO:1].

Blast analysis revealed sequence homology between the AGT-106 cDNA sequence and murine TROY mRNA. TROY is a newly identified member of the Tumor Necrosis Factor Receptor Superfamily (Kojima *et al., J. Biol. Chem. 275(27):* 20742-20747, 2000). Nucleotide sequence homology of ISR TROY with mouse TROY mRNA is 85%.

Hypothalamic AGT-106 expression was decreased with fasting in *Psammomys obesus*. The main effect was observed in group A fed and A fasted animals with an approximately 50% reduction in AGT-106 expression with fasting. This dramatic reduction in AGT-106 expression with fasting was not evident in group B and C animals, and the fed animals in both of these obese groups were similar to the fasted group A animals. These results

demonstrate that hypothalamic expression of AGT-106 in obese animals remains suppressed even in the fed state, suggesting a dysregulation of this gene in these animals.

Interestingly, a significant relationship was also demonstrated between the change in bodyweight after the 24-hour fast (delta bodyweight) and AGT-106 gene expression in the hypothalamus. Although this relationship was seen when all animals were combined, when animals were separated into lean and obese, the association disappeared in the lean animals, but strengthened in the obese groups. There was no relationship between hypothalamic AGT-106 expression and circulating glucose or insulin concentrations.

This demonstrates, therefor, a novel role for Troy (AGT-106), a member of the Tumor Necrosin Factor Receptor Superfamily (TNFRSF) in the regulation of energy utilisation and bodyweight in response to fasting in rodents. As AGT-106 is a receptor in the hypothalamus, a key site within the brain for the regulation of bodyweight and energy balance, this regulation may involve downstream transcriptional regulation of genes involved in homeostasis *via* the NF-κB pathway, or other as yet unidentified pathways. Alternatively, this regulation may involve the action of circulating messengers/molecules feeding back information to the hypothalamus on the state of energy balance within the body. It is proposed that AGT-106 is associated with one or more of mitochondrial dysfunction, myopathy, genetic disorder or cancer.

EXAMPLE 9

AGT-113

AGT-113 was discovered using differential display and it appeared to be expressed at higher levels in the hypothalamus of group C (obese, diabetic) animals than group A (lean healthy) animals.

Real time PCR confirmed this, and showed that group A animals, in both the fed and fasted state, have a much lower expression level of this gene in their hypothalamus than

group B (obese, impaired glucose tolerant) animals and group C animals (A fed v C fed, p=0.031; A fast v B fast, p=0.028; A fast v C fast, p=0.023).

In the fed state, hypothalamic *AGT-113* gene expression correlated with body weight (p<0.001), percent body fat (p=0.002) and plasma insulin levels (p=0.026). In the fasted state, hypothalamic *AGT-113* gene expression correlated with body weight only (p=0.002).

Gene expression in each cDNA sample was quantitated using Taqman PCR technology on an ABI Prism 7700 sequence detector (PE Applied Biosystems, Foster City, CA). Cyclophilin was used as an endogenous control to standardise the amount of cDNA added to a reaction. PCR conditions were 50°C for 2 min, 95°C for 10 min followed by 40 cycles of 95°C for 15 sec and 60°C for 1 min. All samples were assayed in duplicate. For AGT-201 (Example 10), AGT-203 (Example 11) and cyclophilin, fluorogenic probes which had the reporter dye FAM attached to the 5' end and the quencher dye TAMRA attached to the 3' end were used with Taqman Universal PCR Master Mix (PE Applied Biosystems). For AGT-202, AGT-106 (Troy) and *AGT-113*, no probe was used, and SYBR Green Master Mix (PE Applied Biosystems) was used instead. The level of expression of the "house-keeping gene" cyclophilin was examined in each group and was shown not to be altered in the obese, diabetic or fasted state.

Primers used were as follows:

AGT-113:

Forward primer: 5-CATGATGCCAGCCACCTG-3' [SEQ ID NO:16]

Reverse primer: 5'-TCCCAAAGTAAATTAAACACATCAGAA-3' [SEQ ID NO:17]

Cyclophilin:

Forward primer: 5'-CCC ACC GTG TTC TTC GAC AT-3' [SEQ ID NO:18]

Reverse primer: 5'-CCA GTG CTC AGA GCA CGA AA-3' [SEQ ID NO:19]

Probe: 5'- CGC GTC TCC TTC GAG CTG TTT GC-3' [SEQ ID NO:20]

The *Psammomys obesus AGT-113* partial nucleotide sequence is as follows:

TTTCATAGCTGGCATGATGCCAGCCACCTGGCAAACTGTGTCTCTTACCTGACTCCTTTCA
AAATCAAGATATTTTGAGAATAGTCTATATTCTGATGTGTTTAATTTACTTTGGGAAGAAA
CTCCTTGCTTAAGTCTAAAATGGAAAACATTTTTTAATTAATAAAAAAAAAAA [SEQ ID
NO:2].

This sequence has some homology (84% homology over 65 nucleotides) to human clone RP11-368J13 (GenBank accession number AC008070).

The gene expression patterns strongly suggest that *AGT-113* plays a role in body weight regulation and energy homeostasis through its actions in the hypothalamus. *AGT-113* may also be involved in insulin's action or insulin resistance in the hypothalamus. It is proposed that AGT-113 is associated with one or more of mitochondrial dysfunction, myopathy, genetic disorder or cancer.

EXAMPLE 10

AGT-201

AGT-201 was determined to be differentially expressed in *Psammomys obesus* by membrane-based microarray (macroarray) analysis of the hypothalamus.

Primers used were as follows:-

AGT-201

Forward primer: 5'-GCATGCCTGGTTGCCTG-3' [SEQ ID NO:9]

Reverse primer: 5'-TTTCAAGATGGCCTGGCG-3' [SEQ ID NO:10]

Probe: 5'-CCCTGGCAGGTGAGTTCATCAAGGC-3' [SEQ ID NO:11]

The partial nucleotide sequence of *Psammomys obesus* AGT-201 is as follows:

CTTTAAGATT GGGANTNCGA TGATCTCTTG GTGGCAGAGG TGGGAATCTC
AGACTATGGT NCCAAGCTGA ACATGGAGCT NAGTNAAAAG TNCAAGCTGG
TCAAAGAGGN CTACCCAGTG TTNTACCTCT TCCGAGACGG GGACTTTGAG

AACCCAGTCC CATACAGTGG GGCAGTTAAG GTTGGAGCCA TCCAGCGCTG
GCTAAAGGGG CAGGGGGTCT ACCTAGGCAT GCCTGGTTGC CTGCCTGCNT
ACGATGCCCT GGCAGGTGAG TTCATCAAGG CCTCCAGTGT AGAGGCCCGC
CAGGCCATCT TGAAAAAGGG GCAGGAAGGC CTCTCTGGTG TGAAGGAGAC
TGNGAATAAG [SEQ ID NO:3]

Length:360 nucleotides

Analysis of the *Psammomys obesus* AGT-201 sequence showed high sequence homology with human AGT-201 (88%, X94910) and the rat homolog, Erp29 (89%, Y10264).

AGT-201 is known to be located on chromosome 12 and has been mapped to the interval D12S78-D12S79 (12q21-22). 2 animal QTLs are located in the vicinity of AGT-201, Qsbw and Weight1 (Chagnon *et al.*, *Obes Res. 8(1):* 89-117, 2000).

Across the three groups of animals, hypothalamic AGT-201 expression was decreased with fasting significantly in group A and B animals however there was no reduction of expression with fasting in group C animals. These results suggest a dysregulation of hypothalamic AGT-201 expression in diabetic group C animals.

There was significantly lower hypothalamic AGT-201 expression in the fasted animals compared to the fed animals.

AGT-201 gene expression in the hypothalamus did not correlate with body weight, blood glucose or insulin concentration in the fed or fasted state.

These results suggest a role for AGT-201 in the central response to fasting and energy homeostasis, possibly by altering the protein expression, retention, retrieval or folding of secretory proteins exiting the endoplasmic reticulum. In addition, these results suggest that the role of AGT-201 in this regulation may be altered in the diabetic state thereby identifying this gene as a potential target for the development of diabetic treatments. It is proposed that AGT-201 is associated with one or more of mitochondrial dysfunction, myopathy, genetic disorder or cancer.

EXAMPLE 11

AGT-202

AGT-202 was determined to be differentially expressed in the hypothalamus of *Psammomys obesus* by macroarray analysis.

Primers used were as follows:-

AGT-202:

Forward primer: 5'-CTGCAAAACGCCCATTCG-3' [SEQ ID NO:14]

Reverse primer: 5'-TCATAGTCTCGCTCGCAGTAGG-3' [SEQ ID NO:15]

A portion of the *Psammomys obesus* AGT-202 sequence was obtained in order to design primers for gene expression studies.

CCGGAGAGATCATGCACGCCCTCAAGATGACCTGGCACGTGCACTGNTTCACTTGTGCTGC
CTGCAAAACGCCCATTCGCAACCGAGCGTTCTATATGGAGGAAGGGGCACCCTACTGCNAG
CGAGACTATGAGAAGATGTTTGGCACAAAGTGCCGAGGCTGNGACTTCAAGATTGATGCTG
GAGACCGCTTCCTGGAAGCGCTG [SEQ ID NO:4].

Analysis of the *Psammomys obesus* AGT-202 sequence (154 nucleotides) showed high sequence homology with human AGT-202 (88%, L35246) and the rat homolog, AGT-202 (86%, AF096685).

AGT-202 is located on human chromosome 5. No QTL's relevant to obesity or diabetes were found.

AGT-202 gene expression appears to be widespread. cDNA sources include aorta, blood, brain, breast, colon, germ cell, kidney, larynx, lung, muscle, ovary, pancreas, pooled, prostate, stomach, testis, tonsil, uterus, whole embryo, brain, cervix, colon, eye, neck, kidney, lung, ovary, pancreas, prostate, tumor, skin, thymus, pooled, uterus, whole blood

Immuno-localization studies in skeletal muscle using an anti-AGT-202 antibody showed that AGT-202 is present at the Z line and some transverse filaments in adult muscle sarcomeres.

Overall, there was significantly greater AGT-202 gene expression in the hypothalamus of fed animals compared to the fasted animals (p=0.013). In addition, there appears to be greater AGT-202 gene expression in the hypothalamus of Group A and B fed animals compared to Group C animals, however, these differences were not significant. It is proposed that AGT-202 is associated with one or more of mitochondrial dysfunction, myopathy, genetic disorder or cancer.

EXAMPLE 12

Presenilins interacting rhomboid-like protease (AGT-203)

A human gene in the form of an expressed sequence tag (EST) with Accession Number AA131464 was found to be differentially expressed in skeletal muscle of lean, non-diabetic *versus* obese, diabetic animals by membrane-based microarray (macroarray). A human mRNA with a complete coding sequence that matched EST AA131464 was recently added to GenBank (on 1 November, 2000, Accession Number AF197937). The mRNA codes for a 379 amino acid protein they have named Presenilins interacting rhomboid-like protease (AGT-203).

Primers used were as follows:-

AGT-203:

Forward primer: 5'-CCCACCTCTGGAAGAAACTGTCT-3' [SEQ ID NO:6]

Reverse primer: 5'-CCTGTGAACCCAACAGTGAAGA-3' [SEQ ID NO:7]

Probe: 5'-TTATCCTTCCCCCTACCCTATAAGAACTTTGGTG-3' [SEQ ID NO:8]

A portion of the *Psammomys obesus* AGT-203 sequence was obtained in order to design primers for gene expression studies and is provided below:

TGGAAGGTTGAACCTCGAAGATCAGACACAGGGTCAAGTGGTGAAGCTTACAAGAGAAGTGC
CTTGATCCCACCTCTGGAAGAAACTGTCTTTTATCCTTCCCCCTACCCTATAAGAACTTTGG
TGAAGCCCTTTTTCTTCACTGTTGGGTTCACAGGCTGTGCATTTGGATCAGCTGCCATTTGG
CAATATGAATCACTGAAATCCAGGGTCCAGAGTANNTGNNCGGAATGGCAGGAATGCCTGGA
CTCAATGAAATCCAGGGTCC [SEQ ID NO:5].

The AGT-203 gene appears to have a widespread tissue expression pattern. ESTs that correspond to the AGT-203 mRNA have been found in adrenal gland, blood, bone, brain, breast, colon, foreskin, germ cell, heart, kidney, lung, lymph, marrow, muscle, ovary, pancreas, parathyroid, placenta, prostate, skin, spleen, stomach, testis, tonsil, uterus and whole embryo.

The exon/intron structure of the human AGT-203 gene was deduced by aligning the mRNA sequence to human high throughput genome sequencing clones, then applying the GT-AG rule (where all introns start with GT and end with AG). The human AGT-203 gene has 10 exons. The first 4 exons were on clone RP11-315J22 (Accession Number AC068644) which is from chromosome 3. The last 6 exons were on clone RP11-637N15 (Accession Number AC020694) which is from chromosome 17. It is considered likely that one of the clones has been localized incorrectly. Studies are currently underway to determine which is the correct chromosome.

Gene expression studies by Taqman PCR showed a decrease in AGT-203 gene expression in skeletal muscle of obese, hyperinsulinemic group B and C animals when compared to lean group A animals (Group B $p=0.014$, Group C $p=0.011$). This relationship was further supported by a correlation between AGT-203 gene expression in skeletal muscle with log insulin ($p=0.001$), body weight ($p=0.011$) and percent body fat ($p=0.006$). There was no significant correlation with blood glucose levels.

AGT-203 gene expression was found to be reduced in the skeletal muscle of obese, hyperinsulinemic *Psammomys obesus*. A negative correlation was seen with body weight and plasma insulin levels. AGT-203 is thought to interact with presenilin proteins and be involved with protein cleavage.

The presenilins are involved in the proteolytic processing of transmembrane proteins such as APP and Notch. Although APP is most highly expressed in the central nervous system, it is ubiquitously expressed and its role in the skeletal muscle is not known. Diabetes is known to be a risk factor for Alzheimer's disease, and AGT-203 may play a role in both diseases. NOTCH is a membrane receptor and, after proteolytic processing within the membrane, has the ability to move to the nucleus and activate gene expression. AGT-203 may act through NOTCH to affect expression of genes involved in metabolism. Alternatively, the role of AGT-203 in obesity or diabetes may be through processing of another, as yet unidentified, transmembrane protein.

Other possible roles for presenilins include regulation of apoptosis and/or calcium homeostasis. Therefore there are a number of different pathways through which reduced AGT-203 expression could play a role in glucose or fat metabolism in the skeletal muscle, thereby affecting body weight and insulin action. It is proposed that AGT-203 is associated with one or more of mitochondrial dysfunction, myopathy, genetic disorder or cancer.

EXAMPLE 13

Rhomboid-like protein (PSARL) and cancer

A human Cancer Profiling Array II (BD Biosciences) was probed with a ^{32}P-labelled human PSARL probe. The array consists of paired cDNA samples from 19 different tissues including breast, prostate, colon, lung, kidney and liver. Each pair consists of a tumor sample and a corresponding normal tissue sample obtained from the same patient. Twelve of the 19 different tissues have 10 different patients for that particular tissue whilst others have 7 patients (2 tissue types), 5 patients (2 tissue types), 4 patients (1 tissue type) and 3 patients (2 tissue types). As can be seen in the table below, the data generated from the nylon-based array was variable both between tissues and within a given tissue.

Particularly promising results were observed in the breast, kidney and pancreas where the majority of patients exhibited decreased PSARL expression in the tumor compared to the pathologically normal tissue.

A summary of PSARL expression in human tumor tissues is shown below. Data are shown as number of patients for a given tissue with either reduced expression in tumor compared to normal tissue, no change in expression in tumor or increased expression in tumor compared to matched normal tissue. The data are shown in Table 4.

The data in Table 4 provide the levels of expression of AGT-203 in cancer tissue as a percentage of the level in normal tissue. The data represent, therefor, relative expression data of cancer tissue to normal tissue. By "normal" tissue is meant non-cancerous tissue. The number assigned to any one patient is arbitrary and patient 1 for breast cancer is not the same inidividual as patient 1 for kidney cancer, etc.

TABLE 4

Relative expression data of AGT-2003

	Bladder	Breast	Cervix	Colon	Kidney	Liver	Lung	Ovary	Prostate	Rectum	Skin	Small Intestine	Stomach	Testis	Thyroid	Trachea	Uterus	Vulva
Patient 1	58.76%	57.30%	83.78%	91.27%	18.28%	37.57%	141.67%	110.82%	108.72%	188.96%	97.37%	95.80%	106.65%	120.81%	66.37%	44.36%	82.34%	39.95%
Patient 2	47.52%	108.35%	204.11%	126.26%	76.89%	85.44%	125.98%	97.24%	118.32%	92.90%	105.08%	58.30%	67.59%	68.88%	74.34%	221.81%	74.51%	88.24%
Patient 3	124.89%	78.03%	96.79%	98.04%	49.09%	127.46%	138.04%	155.24%	98.55%	113.30%	97.62%	70.45%	72.96%	150.21%	130.57%	57.50%	381.56%	104.10%
Patient 4	171.05%	257.51%	63.48%	69.29%	76.92%		80.78%	243.46%	131.55%	87.54%	174.57%	48.30%	131.82%	53.10%	163.75%		259.77%	73.69%
Patient 5	100.34%	58.24%	122.80%	134.79%	46.43%		97.53%	124.44%		81.14%	154.72%	150.48%	66.45%	74.91%	61.71%		48.74%	66.67%
Patient 6		59.71%	181.83%	114.36%	35.52%		185.00%	144.36%		250.21%	88.66%	47.43%	89.94%	105.06%	94.82%		170.87%	
Patient 7		62.88%	79.06%	87.96%	162.77%		364.85%	104.98%		127.73%	76.25%	93.00%	143.07%	133.11%	109.71%		102.59%	
Patient 8		42.00%	144.63%	98.02%	58.33%		167.37%	80.36%		114.36%	72.76%		114.01%	101.69%	43.66%		108.64%	
Patient 9		109.57%	378.90%	94.45%	88.70%		123.37%	81.20%		105.19%	68.47%		49.76%	169.74%	71.89%		130.88%	
Patient 10		62.74%	151.89%	104.46%	56.79%		184.59%	79.99%		200.77%	104.67%		77.37%	119.96%	73.99%		61.62%	

Those skilled in the art will appreciate that the invention described herein is susceptible to variations and modifications other than those specifically described. It is to be understood that the invention includes all such variations and modifications. The invention also includes all of the steps, features, compositions and compounds referred to or indicated in this specification, individually or collectively, and any and all combinations of any two or more of said steps or features.

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